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Academiae Scientiarum Hungaricae

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Redigit

I. Törő

ABSTRACTS OF THE FOURTH CONGRESS OF THE EUROPEAN SOCIETY OF PATHOLOGY

18-22 September, 1973

Budapest — Hungary

Organized by the

EUROPEAN SOCIETY OF PATHOLOGY
SOCIETY OF HUNGARIAN PATHOLOGISTS
HUNGARIAN ACADEMY OF SCIENCES

Akadémiai Kiadó, Budapest
1973

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Preface

This collection of summaries of papers accepted for presentation at this Congress has been published with the aim to make your participation more profitable and your work more efficient. All topics are listed in the table of contents of this brochure. By using the author index you may find the abstract and locate the lecture in the programm.

PATHOLOGY OF THE ARTERIES

with special regard to non arteriosclerotic diseases, as regeneration, transplantation, problems of permeability, inflammative changes etc. in experiments and in humans.

Organized by

JELLINEK, H.

PROBLEMS OF PERMEABILITY

Invited lecturers

ADAMS, C. W. M.
CONSTANTINIDES, P.
GABRYEL, P., BICZYSKO, W.
JELLINEK, H.
KLEMPERT, H., KALIFAT, S. R., DIEBOLD, J.
KUNZ, J.
LINDNER, J.
OONEDA, G.
RONA, G., HÜTTNER, I., MORE, R. H.
WEBER, G.

PROTEIN AND LIPID ENTRY IN ARTERIES

C.W.M. Adams, Department of Pathology, Guy's Hospital Medical School, London, U.K.

Previous immunological, immunofluorescence and immuno-electrophoretic evidence has revealed lipoproteins in the arterial intima. By contrast, influx studies indicate that cholesterol which accumulates in the normal arterial intima cannot be entirely derived from lipoprotein; the free/esterified cholesterol ratio in the accumulated lipid is quite different to that in low-density lipoprotein from plasma. Our own studies show that most plasma protein enters the normal rabbit aortic wall from its outer surface, but - when the intima is damaged by the development of atheroma - the entry gradient reverses and most protein enters from the intimal surface. Related studies on other arterial diseases show that plasma-protein is markedly increased when the wall is dammaged by a variety of insults. Collectively, these observations accord with Zilversmit's view that the intact endothelium forms a barrier to the entry of plasma lipoprotein.

Cholesterol that has been deposited in the arterial wall as an atheromatous lesion appears to be metabolically inert, at least in the rabbit. Lipoprotein in the arterial wall may or may not be in equilibrium with that in plasma. The deposited cholesterol forms an inert third pool, which does not equilibrate with lipoprotein cholesterol.

INCREASE OF AORTIC PERMEABILITY IN HYPERCHOLESTEROLAEMIC RATS. ELECTRON MICROSCOPIC STUDY.

Bálint,A., Veress,B., Kerényi,T.,Jellinek,H.
2nd Department of Pathology of Semmelweis Medical University, Budapest.

Female rats were given an atherogenic diet /Loustalot,P., Helv.phisiol.Acta,1960, 18:343/. The animals were sacrificed 10, 21, 42 and 63 days after the beginning of the experiment. Parts from the thoracic and abdominal aorta were examined under electron microscope. Vascular permeability was followed-up by colloidal-iron tracer method /Veress et al, Atherosclet., 1970, 11:369/. To examine the endothelial external coat /glycocalyx, surface coat/ the ruthenium red fixation /Brooks,R.E., Stain. Technol., 1968, 44:173/ was used.

In hypercholesterolaemic rats increase of vascular permeability preceeded lipid accumulation and structural changes in the aortic wall. Decrease of electron density as well as of thickness of the endothelial external coat was observed in the same experimental groups. The role of these findings in the pathogenesis of aortic lesions /atheroma/ is discussed.

ELECTRON MICROSCOPIC-AUTORADIOGRAPHIC STUDY OF LIPOPROTEIN ENTRY INTO ARTERIES

Constantinides, Paris
Department of Pathology, Medical School, University of B.C., Vancouver, Canada.

The movements of labelled lipoproteins into the arterial wall of a) normal, b) hyperlipemic-atherosclerotic, c) DOCA-treated, and d) serum-sick rabbits were visualized autoradiographically by giving 15 mCi per kilogram ^{3}H-cholesterol, spread in 5 daily doses, by stomach tube to several rabbits in each of these 4 groups. The animals were killed 6 hours after the last ^{3}H-cholesterol feeding, and thick sections from their glutaraldehyde-digitonin-fixed aortae, coronaries and other tissues were then coated with a photographic emulsion, exposed for 2-6 months and examined electron microscopically. It was found that in normal animals only a negligible number of labelled lipoprotein molecules crossed the arterial endothelium, but large numbers of them crossed the capillary endothelium in the myocardium and liver. By contrast, the arterial endothelium of hyperlipemic-atherosclerotic, DOCA-treated and serum-sick animals proved highly permeable to lipoproteins, allowing them to cross freely into the arterial wall. Transendothelial label transport was mainly trascytoplasmic (and probably transmembrane) but some label also crossed through opened juctions. These results show that the normal arterial endothelium - unlike that of certain capillaries - has an extremely low permeability for large lipoprotein molecules but that protracted hyperlipemia, hypertension and immune insults make it highly permeable to these molecules.

THE IN VITRO INCORPORATION OF ^{125}I-LABELLED BETA-LIPOPROTEID INTO THE RABBIT AORTA /A SUPPORT FOR THE HEMODYNAMIC CONCEPT?/

Dénes, Róbert; Virág, Sándor; Stützel, Mária and Kóczé, Antal
Semmelweis University of Medicine, IIIrd Department of Medicine, Budapest, Hungary

In our previous study we were able to correlate the incorporation of labelled beta-lipoproteid with the species differences in susceptibility towards experimentally induced atherosclerosis. According to the hemodynamic concept the distribution of atheromatous plaques in the aortic wall might be connected with hemodynamic factors. For that reason it seemed to be relevant to investigate the possible role of hemodynamic factors in the incorporation of labelled beta-lipoproteid in order to evaulate whether or not the hemodynamically predilected areas would exhibit a greater rate of incorporation as compared with the hemodynamically unaffected areas. Aortas of normal rabbits were used in an in vitro system for testing the rate of incorporation of the labelled beta-lipoproteid. After having been the incubation with labelled material completed, the aortas were cut into several areas according to a previously established scheme based on a postulated influence of hemodynamic factors. The radioactivity of each area was expressed as count/min/mg dry tissue. The results obtained indicate a clear cut correlation between the hemodynamic pattern and the incorporation of labelled beta-lipoproteid.

EFFECT OF TRANSITORY HYPOXIA ON THE PERMEABILITY OF RAT AORTA. AN ELECTRON MICROSCOPIC STUDY.

Gabriella Elemér, Horváth,G.,Jellinek,H., Kerényi,T., 2nd Dept.of Pathology, Semmelweis Medical University, Budapest-Hungary.

In the early phase of arterial lesions the penetration of plasma into the vessel wall is an important process. In the presen study transitory hypoxia was produced mechanically by double ligation for one hour of the abdominal aorta's infrarenal part.Changes in the permeability were studied electronmicroscopically at different points of time from one hour to 13 days following recirculation using colloidal iron /Ferrlecit/ as a tracer. Increased permeability was demonstrable already in the first hour of recirculation. The tracer substance appeared in the pynocytotic vesicles and in the intercellular junctions. On the second day the permeability increase reached its maximum. At this time the tracer was demonstrable partly in the organelles, partly freely in the cytoplasm of all cellular components of the vessel wall. Simultaneously the smooth muscle cells exhibited various degrees of degenerative changes up to the osmiophilic necrosis. From the second day of recirculation on the intensity of changes decreased and after one week no changes were demonstrable at all.

^{131}J-ALBUMIN IN THE AORTA AFTER ANGIOTENSIN AND DIVASCAN.

Fuchs,U.,Gepp Dugula, Wiegershausen,B.,Rieth ling Anna-Kathrin, Loebe,J., Inst.of Pathology,Radiological Clinik,Karl-Marx-University, Leipsig-GDR; Inst.of Pharmacology and Toxicology, University, Rostock-GDR.

A short term hypertension augments the Imp./min/10 mg wet weight measured in the aorta of the rabbit. The effect of Divascan was examined. Divascan is an Adrenochrom-derivative and diminishes the permeability of the skin of rats after application of histamine, serotonin and kinins.
Results: the blood pressure of the rabbits was raised by 57-9 Torr after angiotensin II. The measured activity of the aorta was raised in these animals by 4,5 times.The animals, which wer given Divascan and Angiotensin II, had values lying between those of the controls and the hypertensive rabbits depending upon dose of Divascan. These results apply to all 15 segments of the aorta. The activity of the single segments demonstrates higher values for the arch of the aorta and to some degree for the proximal abdominal region. The sections show the greatest activity in the outer parts of the aorta as shown by Adams,Morgan and Bayliss /1970/. Conclusions: elevation of blood pressure for a short time augments the activity of ^{131}J albumin in the aorta after Angiotensin and Divascan.

THE PERMEABILITY OF CEREBRAL CAPILLARIS OF THE NEWBORN RABBITS BY MEANS OF PEROXIDASE AS A TRACER.

Gabryel,P., Biczysko,W., Inst.of Biostructure, Dept.of Pathological Anatomy, Posnan-Poland.

Horseradish peroxidase in physiological solution was administered into newborn rabbits intracardially or intravenously in the amounts of 10 mg per 25 g body weight on the 2nd,3rd,5th,8th,12th and 18th day.Animals were sacrificed 20 and 40 min. after the injection. Specimens of frontal cerebral lobes were examined according to the technique given by Karnovsky.
In the rabbits up to the 8th day the blood-brain barrier was permeable for peroxidase. Its transport takes place by means of micropinocytosis through gaps between endothelial cells and through invagination of their cytoplasmic membrane. Reactions products were found in basal membrane of capillaries, in astrocyte feet and in the pericellular space and in the neurons. Between the 12th and the 18th day the barrier becomes tight for peroxidase in a similar way as it takes place in adult animals.Peroxidase becomes confined to the lumen of the capillaries,intercellular junctions of endothelial cells do not permit leakage of the enzyme,the micropinocytotic transport was very slow.The current study indicates gradual maturation of the blood-brain barrier in newborn rabbits.

NOUVELLE THÉRAPEUTIQUE DANS LES AFFECTIONS VASCULAIRES AVEC OU SANS TROUBLES DE LA PERMEABILITÉ CAPILLAIRE.

Gazave,J.M., Labor.de Physio-Pathologie, Faculté de Médecine, Paris-France.

THE PATHOGENESIS AND HEALING OF ARTERIOLAR DAMAGE IN EXPERIMENTAL HYPERTENSION IN THE RAT

F.S. Goldby
K.R.U.F. Institute of Renal Disease, The Royal Infirmary, Cardiff, Wales.

Arteriolar damage in the form of fibrinoid necrosis is the pathological hallmark of malignant hypertension. The pathogenesis of the lesion is the subject of controversy. The results of an electron-microscopic and experimental study of the gut arterioles of rats made hypertensive by angiotensin infusion or renal artery constriction is reported. Nephrectomized rats infused with angiotensin developed arteriolar dilatations which were permeable to colloidal carbon particles. Electron microscopy showed endothelial damage in the dilated segments with deposits of amorphous material and carbon particles displacing muscle cells in the media after one hour of hypertension. The arterioles of rats with renal clip hypertension also showed dilatations permeable to carbon particles which were situated in similar lesions in the media. Intimal thickening in dilated segments appeared to follow medial damage. In healing lesions carbon particles in the media were phagocytosed by smooth muscle cells. It is suggested that a rapid rise in arterial pressure causes patchy arteriolar dilatation, endothelial damage and flow of plasma into the media and subsequently the intima. When pressure is lowered the plasma deposits are removed by smooth muscle in the media and macrophages in the intima.

PERMEABILITY DISTURBANCES OF POSTISCHEMIC AORTAS.

Horváth,G., Kerényi,T., Kurunczi,S., Detre, Z., Jellinek,H.
2nd Department of Pathology of the Semmelweis Medical University, Budapest.

In order to examine the postischemic permeability disturbances of arteries of elastic type, rat abdominal aortas have been compressed for one hour and recirculated for periods of 1 hour to 30 days. To trace the permeability, colloidal iron preparation /Ferrlecit®/ was used, given one hour before killing the animals. Histological examinations revealed the most severe permeability disturbances on the second-third day of recirculation. The increasing of permeability showed parallelism with the damages of the medial cells. The quantitative microanalysis of iron content in the different aortic samples gave the diagram of the permeability for the whole aortic wall.

SOME NEW ASPECTS OF THE METABOLIC PROCESS OF THE ARTERIAL WALL.

H.Jellinek, 2nd Dept.of Pathology, Semmelweis Medical University, Budapest - Hungary

Three different methods were applied to the study of material transport through the vessel wall under different experimental conditions. The colloidal iron tracer method developed in this Institute was applied successfully for both light- and electron microscopic studies. It was shown, that in animals fed on high-lipid diet, the tracer appeared in the vessel wall earlier than the lipid uptake became demonstrable by electron microscopy. The role of macrophages in the trans-vessel wall transport was also examined.
The importance of lymph-vessels was shown particularly under pathological conditions in the drainage of material penetrated into the arterial wall. The localisation and modification of alcaline phosphatase activity was also studied and its regeneration observed. Changes of the thickness of the external coat were examined under different experimental conditions. The damage caused to the vessel wall by the transport of materials was pointed out and the morphological similarity of the regenerative processes and the arteriosclerotic changes was emphasized.

CARBON MONOXIDE AND ARTERIAL PERMEABILITY Ultrastructural studies after injection of various tracers.

Kjeldsen, K. and Klem Thomsen, H.
Department of Clinical Chemistry A Rigshospitalet, Copenhagen, Denmark

Rabbits exposed to 180 ppm carbon monoxide for 2 to 4 hours were at the end of the experiment given ferritin, Intralipid®, or carbon black. A significant increase in endothelial permeability was seen in the experimental animals. The tracer particles entered the subendothelial space via the interendothelial junctions.

ULTRASTRUCTURAL STUDY OF THE ALVEOLAR-CAPILLARY MEMBRANE PERMEABILITY TO PEROXYDASE (HRP) IN THE RAT.

Klempert H., Kalifat S. R., Diebold J.:
Laboratoire de Microscopie électronique
C. H. U. Broussais-Hôtel-Dieu
U. E. R. Biomédicale des Cordeliers,
Paris (France)

This study was undertaken to investigate the mecanisme of formation and resorption of interstitial and alveolar pulmonary edema. In many animal species including the Rat, HRP induces release of vasoactive amines increasing the capillary permeability. Rats weighing 100 g were injected intravascularly with the following doses of HRP: 1, 5, 15, 20, 30 mg at intervals of 1, 2.5, 5, 6, 10, 15, 30, 60 min. Results were compared when fixation-perfusion was used. Increase of capillary permeability was maximum with high doses of peroxydase after 15 min. The alveolar lining epithelium was also permeated by the HRP. The capillaries showed opacification of the lumen, pinocytic vacuoles, intercellular spaces and basement membrane. The intercellular spaces of the alveolar lining and the pinocytic vacuoles were also opacified. In the lumen macrophagic cells showed vacuoles containing peroxydase. HRP was also observed on cell surface in the lumen.

NEW IN VITRO METHOD FOR THE INVESTIGATION OF VESSEL WALL PERMEABILITY

Kóczé, Antal; Virág, Sándor; Stützel, Mária and Dénes, Róbert
Semmelweis University of Medicine
3rd Department of Medicine
Budapest, Hungary

The uptake of isotope labelled substances in surviving vessel disks has been examined by several authors. The previously applied in vitro methods did not allow the differentiation of the adventitial and intimal inflow of the substances. Our experiments were performed on surviving aortic disks of rabbits with labelled albumin and beta lipoprotein. The adjoining intimal and adventitial surfaces were stuck together by a tissue adhesive applied in human surgical practice. Prior to the experiment the animals underwent various procedures resulting in different types of aortic lesions. This method furnished the means of the selective examination of transintimal and transadventitial inflow. According to our experiences both in normal and altered aortic disks the transadventitial uptake is more intensive than the transintimal one and it is an active process. On the other hand the transintimal uptake is dependent on the grade of the tissue disturbance and can be influenced by substances acting upon the vessel wall permeability.

VASCULAR LESIONS IN ACUTE HYPERTENSION IN THE RAT.

I.Kolonics, Éva, Konyár, T.Kerényi, H.Jellinek.

Lesions of the aorta and the small muscular type arteries were studied in acute local or general hypertension in the rat. Local hypertension was made by ligation of the abdominal aorta, while the general one by the administration of norepinephrin. Already a 10 minutes period of hypertension was found to have exalted the permeability of the endothelium of the aorta and the coronary arteries as revealed by the colloidal iron tracer technic. Lesions of the different types of vessels were compared in local and general hypertension.

AUTORADIOGRAPHIC STUDIES OF CHANGES IN THE PERMEABILITY OF THE VASCULAR WALL IN EXPERIMENTAL HYPERTENSION

Kunz, Jochen

Pathologisches Institut der Humboldt-Universität, Isotopenabteilung, Berlin, DDR

The permeability of the vascular wall of rats with renal hypertension for ^{125}J-Fibrinogen and ^{125}J-Albumin was studied autoradiographically. Intramural and perivasal deposits of these plasmaproteins were found in terminal regions of the vascular syster of myocard, cerebrum, mesenterium and kidneys in hypertension, but not in controls. In these organs many small arteries with and without structural changes show the same deposits. Therefore a correlation between these foundings and the progredience of hypertonic angiopathy seem to exist. After the application of ^{125}J-Albumin no differences were found in radioactivity of different layers of the aortic wall and in the serum of normotonic and hypertonic rats. The prefered attack of small arteries and arterioles in hypertension is explained by the increased hydrodynamic loadings and by structural and metabolic specialities.

NEW RESULTS ON METABOLISM OF ARTERIAL CONNECTIVE TISSUES

Lindner,J., and G.Johannes
Inst.of Pathology, Univ.of Hamburg,FRG.

Metabolism of arterial connective tissue is highest postnatal, decreases with maturation and ageing /in mammalians, humans included/, using the DNA-content as parameter for some metabolic rates. Investigations on human arteries after classification in 4 arteriosclerosis stages in comparison to morphologically unchanged parts of the same vessel wall an classification in age groups show that atherosclerosis starts with an enhanced anabolism. The primary synthesis of ground substance is combined with an enhanced O_2-consumption. The fibre synthesis starts later. The increased anabolism ist followed by an increased catabolism. The turnover rates of connective tissue components are enhanced therefore. Then both processes decrease, catabolic more than anabolic ones; Autoradiographic and radiochemical analyses show that synthesis rates of groundsubstance are higher in intima than in media of all atherosclerosis stages, Quantitative immunological analyses demonstrate the highest serum protein contents in oedemateous plaques at the same time. The summarizing synopsis show the changes of metabolic rates of arterial connective tissues in atherosclerosis and ageing.

PLASMATIC ARTERIONECROSIS, AS THE CAUSE OF HYPERTENSIVE INTRACEREBRAL HEMORRHAGE

OONEDA, Genju
Department of Pathology, School of Medicine, Gunma University, Maebashi, Japan

In autopsy cases of hypertensive intracerebral hemorrhage and hypertension the morphogenesis of the vascular lesion, which was considered to be the immediate cause of the hemorrhage, was morphologically studied. The direct cause of the hemorrhage was the rupture of the intracerebral microaneurysms resulted from the plasmatic arterionecrosis of the intracerebral arteries. The arterionecrosis was predominantly present in the arteries of about 150 μ diameter, especially in the external branches of the arteriae corporis striati mediae in the putamen, and characterized by medial smooth muscle cell disappearance, blood plasma insudation in the intima, histolysis of the internal elastic lamina and intimal collagenous fibers, fibrin deposition (fibrinoid degeneration) in the intima, and luminal dilatation. The morphogenesis of the arterionecrosis was the development of histolysis as well as fibrinoid degeneration caused by blood plasma insudation in the wall of the arteries with preceding necrosis and disappearance of medial muscle cells. Intracerebral microaneurysms were also formed by the plasmatic arterionecrosis in a narrow sense, in which histolysis due to blood plasma insudation had occurred, but fibrin deposition in the intima had not yet arisen. Medial muscle cell damage resulted in the luminal dilatation of the arteries, and then this was followed by fibrous intimal thickening. It was in the intimal thickening with dilated lumen, but not in that with narrowed lumen, that blood plasma insudation, i. e. the arterionecrosis developed frequently.

STRUCTURAL AND FUNCTIONAL CORRELATES OF PROTEIN TRANSPORT IN ARTERIAL ENDOTHELIUM. Rona, G., Wüttner, I., and More, R.H., Pathology Department, McGill University, Montreal, Canada.

Our investigations that disclosed the presence of incomplete tight junctions and gap junctions in arterial endothelium (J. Cell Biol. 1973, Lab. Invest. 1973) gave further morphologic support to the view that protein molecules enter arterial subendothelium via two selective pathways: intercellular clefts and vesicular transport. Significant regional differences were shown to exist in permeability to protein tracers in various arterial segments of normotensive rats, which correlated with dissimilarities in the fine structure of endothelial cell junctions. The present work was designed to study effects of blood pressure levels on passage of protein tracers through selective endothelial pathways. High and low arterial blood pressures were induced by infusion of catecholamines (norepinephrine and isoproterenol) and by mechanical means (aortic coarctation) in Sprague-Dawley rats. While monitoring blood pressures by polygraph, protein tracers (horseradish peroxidase and ferritin) were injected intravenously and localized later in the intima of selected arterial regions by electron microscopy. Results indicated that within a blood pressure range of 60-220 mmHg, passage of protein molecules is influenced by the blood pressure level along both selective pathways, but is modified by regional differences in permeability to fine-structural protein tracers of arterial endothelium. At very low blood pressure levels (20-30 mmHg) protein tracers entered arterial subendothelium in a striking amount indicating loss of macromolecular barrier function in the endothelium. (Supported by MRC Grant #MT 3683).

FINE STRUCTURAL CHANGES OF BRAIN CAPILLARIES IN CATS INFECTED WITH PROCANDIDA ALBICANS

Szücs,A. and Joó,F.+
Brain Research Institute, Medical Univ. and Biol. Res. Center+,Szeged,Hungary

Although the number of cases of mycotic infections of the central nervous system /CNS/ have considerably increased during the past decades, there are but few experimental reports on the pthogenesis of meningoencephalitis caused by Procandida albicans /Pc.albicans/.

Primary infection of the CNS could be readily performed by means of intracarotical injection of $2x10^6$ living cells, after washing in saline, of Pc. albicans culture. 2,4,12 and 24 h after injections, cats were perfused with Karnovsky's fixative /pH 7,4/ for 30 min, postfixed in buffered osmic acid solution and embedded in Durcupan /Fluka/.

Pathological changes of brain capillaries consisting of an increase in pinocytosis, swelling of endothelial cytoplasm and induction of phagocytosis of endothelial cells, were found to have developed earlier and in more severe form than that of infection caused by other authors with intravenous injection.

ULTRASTRUCTURAL OBSERVATIONS ON AORTIC ENDOTHELIAL SURFACE IN EARLY CHOLESTEROL EXPERIMENTAL ATHEROGENESIS AND UNDER THE INFLUENCE OF METHIL PREDNISOLONE IN NORMAL AND CHOLESTEROL-FED RABBITS.

Weber,G., Inst.of Pathological Anatomy of University, Siena-Italy.

Endothelial aortic surface of grown-up guinea pigs, rabbits and rats is cowered with a Concanavalin-A reactive coat. This coat in early experimental cholesterol atherogenesis in rabbit, shows at first a remarkable increase in its thickness/from 180-200 Å to about 0,6 micron/ while later on it disappears. Where endothelial surface has lost its reactivity to Concanavalin-A, a deposition takes place of plasmatic material admixed with circulating cells. In suckling rabbits, at the 15th day from birth, this coat, which is not to be seen at birth, is well evident, though very blender, on endothelial aortic surface.

THE PROBLEMS OF THE REGENERATION

Invited lecturers

ANESTIADI, B.
BJÖRKERUD, S.
HAUST, M. D.
HOFF, H. F.
KÁDÁR Anna
KNIERIEM, H. J.
LEU, H. J., BRUNNER, U.
RANNIE, I.
WALTON, K. W.

PHYSICAL AND CHEMICAL CHARACTERISTICS OF ARTERIAL ELASTIN.

V.Anestiadi, Kishinev,USSR.

The functional disorders of arteries affect already in their early phases the physico-chemical characteristics of elastin. These are shown by specific modifications of the type and intensity of fluorescence. The intensity changes may cover the complete range from hardly realizable to marked fluorescence. Paradoxical effects of elastase my simultaneously occur.

An increase of lysine content was frequently observed while the monoamino-oxydase activity decreased progressively. The impaired oxydation of lysine results in the inhibition of desmosine, isodesmosine formation and ulti ately in the poor elasticity and stability of elastic fibres.

A definite age dependence was observed of the metabolic and compensatory abilities of the arteries.

MORPHOLOGICAL STUDIES ON EXPERIMENTAL ARTERIAL SUBSTITUTES PREFORMED " IN SITU "

Bartos,Gábor,Kádár,Anna and Mayer,Ferenc
2nd Department of Surgery, Pécs, Medical University and 2nd Department of Semmelweis Medical University, Budapest,Hungary

In a two steps operation a silastic tube wraped in a polyester meshgraft had been inserted into the vicinity of the abdominal aortic segment of dogs. The implant was incorporated into the host within 6 to 8 weeks. A "living" auto-alloplastic tube with an own blood supply developed around silicon mandvel which was removed at the second operation, and the graft was anastomosed to the cut ends of the aorta.

The fate of these arterial substitutes had been followed up to 3 years by means of light- and electron microscope. The wall of the grafts had transformed in a new structure that resembled to the arterial wall. Endothelium, smooth muscle cells and elastic fibers developed in a great number even in the long term specimens. There were only a few degenerative changes in these grafts.

On the basis of the morphological characteristics this type of in situ graft is of high biological value. It seems to be nearly equivalent to the autologous vein graft and to be superior to all the other grafts.

THERMOANALYTICAL INVESTIGATIONS ON THE REPAIR REACTIONS OF THE ARTERIAL WALL

Bihari-Varga,Magdolna

IIIrd.Department of Medicine,Semmelweis Medical University,Budapest,Hungary

Repair processes were studied in the arterial wall of two groups of animals:
1./ in rabbits recovering from experimental lathyrism, and
2./ in rabbixs previously exposed to hypoxia

Applying a complex thermoanalytical metnod,the derivatography, changes in the amount of structural water-, and glycosaminoglycan-content could be measured and alterations in the synthesis of fibrillar proteins could be demonstrated.

The defect in the synthesis of the aortic fibrillar proteins of growing animals kept on latnyrogenic diet proved to be only partly reversible.

Reparative reactions following 12 hour hypoxia resulted in the elevation of glycosaminoglycan contents significantly correlated with an increased rate of collagen and elastin synthesis within the aortas of the experimental animals.

REPAIR REACTIONS OF THE ARTERIAL WALL IN RELATION TO ARTERIAL DISEASE

Björkerud, Sören
Arterial Biology Section, Dpt of Medicine I, University of Göteborg, Göteborg, Sweden

Sequential changes following different types of defined mechanical injury to the rabbit aorta were studied. By means of a microsurgical instrument 3 different types of injury were induced in the aorta of living rabbits: (1) superficial injury with small area, (2) total local necrosis, and (3) superficial injury with large area. The response after each specific injury was characterized by a different set of changes: (i) superficial injury with small area - intimal thickening with rapid reendothelialization without accumulation of lipids and leading to healing; (ii) the induction of a total local necrosis - calcification, encapsulation, and capillarization, and (iii) superficial injury with large area - intimal thickening, delayed reendothelialization with accumulation of lipids and formation of mural thrombi.

Comparisons between human arterial lesions and the experimental lesions suggest that progressive intimal thickening in the human may be a physiological repair response following subtotal arterial wall damage; medial (Mönckeberg) sclerosis may represent a direct tissue response to total injury with necrosis; and atherosclerosis may be a combination of 3 different responses to 3 different stimuli, i.e. subtotal injury (intimal thickening), delayed reendothelialization (accumulation of lipids, mural thrombi), and, in advanced lesions foci with total tissue injury (calcification, encapsulation, capillarization).

EFFECTS OF GLUCOCORTICOIDS ON CELL PROLIFERATION OF THE ARTERIAL WALL.

C.Cavallero, U.Di Tondo, S.L.Giusto, Inst. of Pathological Anatomy II. University of Rome-Italy.

In autoradiographic studies carried out with ^{3}H thymidine, cholesterol-fed rabbits were treated for different periods of time with several natural or synthetic steroids, including cortisol, prednisone, dexamethasone, desoxycorticosterone, aldosterone, pregnenolone, progesterone, testosterone and others, in order to study their effect on cell proliferation in the atherosclerotic plaques. It was found that natural and synthetic glucocorticoids with antiinflammatory activity lower the ^{3}H thymidine incorporation in the plaques, while mineralocorticoids seem to increase it. Increased rates of radioisotope incorporation were observed after testosterone, pregnenolone and progesterone too. A close relationship seems to exist between the dose of the glucocorticoid employed and the inhibitory effect on cell proliferation. This effect may be due to changes in arterial lipid metabolism and/or to changes of activity of lysosomal enzymes induced by the steroid. It is well known that in the rabbit, in spite of an increased level of serum lipids, glucocorticoids greatly decrease the intensity of cholesterol atherosclerosis; this effect may be related, at least partly, to the inhibition of cell proliferation in the arterial wall.

MORPHOLOGY OF CULTURED ENDOTHELIAL AND SMOOTH MUSCLE CELLS OF DIFFERENT ORIGIN.

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It has been shown by us previously that essentially identical histological lesions are developed in the arteries by hypertension, anoxia, cholesterol feeding etc. This apperent non specific reaction of the arterial wall suggested the uniformity of cellular response to a variety of damages. This may be studied in model experiments on in vitro cultured pure lines of the main cell type involved in the arterial reaction. Methods were developed to obtain homogenous lines of endothelial and smooth muscle cells freshly removed chicken aortas, amnion, and gizzard, rat aortas and uterus, human uterus and porcin aortas. The identity of cells was verified by their cell culture morphology and biology using light microscopy and in certain cases chromosome analysis. Ultrastructural characteristics were studied by electronmicroscopy.

VASCULAR MODIFICATIONS IN EXPERIMENTAL HIPOCUPROSIS IN CHICKEN

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Vascular modifications were investigated over a period of 56 days in Studler Chicken fed on semi-purified copper-deficient diet based on creamed powder milk, with and without copper supplement. After slaughtering, the main vessels were collected. The histopathological examination was done on samples coloured with azan-Heidenhein, Weigert, Gordon-Sweet, Hotchkiss-McManus and Müller reactions. The following modifications were ascertained: a moderate fibrosis of the media, elastolysis with fragmentation of lamellae and fibres; the reticulin was densified through agglomerated, partially colagenised fibres; accumulation of acid mucosubstances and PAS positive matter in endothelium, in sub-endothelial layer and in the inner half of media. Elastolysis is considered as a consequence of copper deficiency inducing a reduction of the amino-oxydasic activity.

INTIMAL CELLS IN FIBRILLOGENESIS

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Until recently it had not been known or accepted that the intimal cells involved in all stages of atherosclerotic lesions were smooth muscle cells. Thus it has been shown that many of the fat containing cells in fatty streaks are smooth muscle cells, and in the fibrous plaques smooth muscle cells, being the only cell element, are responsible for connective tissue proliferation. The latter is not an isolated feature in atherosclerosis as in developing vessels of man and animals smooth muscle cells do elaborate connective tissues from the earliest stage. The connective tissues produced by these cells include all forms of formed elements, i.e. the microfibrils of the extracellular space, the collagen and units of elastic tissue. The process of fibrogenesis by smooth muscle cells is similar during periods of development as well as under normal and pathological conditions. However, there may be subtle differences presently explored in part in tissue culture. These include not only the fine structure of some connective tissues but perhaps also some aspects of cellular proliferation in the intima (and inner media).

VASCULAR INJURY.

Hoff,H.F., Max Planck Institut, München-GFR

CELLULAR REACTIVITY IN EXPERIMENTAL DIFFUSE INTIMAL THICKENING AFTER MECHANICAL CHEMICAL, HYPOXIC AND IMMUNOLOGICAL ARTERIAL INJURIES.

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Cardiol. Res. Center, Boucicaut Hosp. Paris. Med. Acad Sofia ;Dept. Pathol. St. Antoine Hosp. Paris.

Diffuse intimal thickening (DIT) has been induced in elastic/muscular arteries of rats (double ligature, formol treatment) and of rabbits (periarterial plastic tube, heterologous aortic immunisation) ; comparative histological, histochemical and electron-microscopical studies were carried out. The DIT's frequency, chronology, spread and rate of growth varied from one experimental group to another ; nevertheless the ultrastructure and the histoenzymatic equipment of the cells in all the cases examined correspound to those of the "modified" smooth muscle cells ; only in some superficial areas cells with the histoenzymatic characteristics of endothelial cells are observed. The high activity of the respiratory and glycolytic enzymes, the pyroninophilia and the metachromasia as well as the intensity of the MPS-linked enzymes suggest an increased synthesis of proteins and MPS, obviously connected with an active cell proliferation. These morphological and metabolic similarities seem to express a general reaction of the arterial medial and endothelial cells, related to a phenomenon of structural and functional adaptation to various agressions.

THE ULTRASTRUCTURE OF THE ELASTIC TISSUE.

Kádár, Anna, Dept. of Pathology, Semmelweis Medical University, Budapest-Hungary.

The elastic fibre formation is morphologically identical under normal and pathological conditions. The elastic fibre consists of aggregats which are composed of microfibrils, elastin-protein and mucopolysaccharides. The elastic material is produced by the smooth muscle cells in the aorta wall.

The microfibrils consists of glycoproteins and glycosaminoglycans. The proteins are different that of the elastin protein. The formation of elastic tissue might be inhibited in experiments by copper deficiency and by administration of betaaminopropionitrile. These conditions resulted the inhibition of the polymerization of elastin from tropoelastin and therefore the development of normal elastic fibres.

The glycoprotein and glycosaminoglycan components of the elastic tissue exhibit ruthenium red positivity. The different constituents of the elastic fibres can be easily differentiated by elastase digestion.

Elastins purified by different biochemical methods - in collaboration - from bovine ligamentum nuchae and porcine aorta revealed similarity to the in vivo elastic material. The protein elastin has a granular-fibrillar structure, the microfibrils form a network. Different electron microscopic methods were used for the characterization of the elastic tissue.

THE ROLE OF SMOOTH MUSCLE CELLS IN REPAIR AND REGENERATION OF THE ARTERIAL WALL

Knieriem, Hans-Jürgen
Department of Pathology, University of Düsseldorf, West Germany (GFR).

Different kinds of injuries of the arterial wall will initiate a similar proliferation of vascular smooth muscle cells which may differ in its properties but results in the repair of the vascular wall defects. Although both the intimal and medial smooth muscle cells are responsible for the reparative process, they will not be able to restore complete integration of the wall architecture. The additional formation of ground substance, collagen and elastic fibers and even of foci of calcifications demonstrate the significance of the scar-like changes The various ultrastructural properties of the reparative process will be discussed in relation to two experimental models: injury of the rat carotid artery after clamping and treatment with formalin and of the rabbit aorta after transverse mechanical laceration of the intima. The results of our experimental studies will be compared with those of other types of injuries, in particular of changes observed after surgical procedures of the arterial wall. The final molding and the fate of the reparative and regenerating process of the arterial wall will depend on the different hemodynamic and metabolic conditions and may promote secondary degenerative and even atheromatous lesions.

EXAMINATION OF HYPERTENSIVE VESSEL LESIONS BY THE RUTHENIUM RED METHOD.

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Luft's ruthenium red method was used to study the electron histochemistry of acid mucopolysaccharides in hypertensive lesions of muscular and elastic type arteries of albino rats. The continuity of the ruthenium red positive external coat on the luminal face of endothelial cells remained intact for to 17 days in hypertensive animals.The increased permeability observed in this period was possibly the result of the opening of intercellular junctions since no exalted transcellular transport was demonstrable. The resulting plasma accumulation and fibrin precipitation was uniformly present in both types of arteries.

Morphologically the intima proliferation was the same in lesions caused by hypertension or other damages i.e. smooth muscle cells of different ergastoplasmatic contents accumulation RR positive mucopolysaccharides and the production of elastic fibres.

In the media of both types of arteries the amount of RR demonstrable mucopolysaccharides increased considerably. Simultaneously the morphological signs of exalted metabolism became apparent in the medial cells. Also the adventitial granulation tissue was shown to produce mucopolysaccharides.

ULTRASTRUCTURAL STUDIES ON HUMAN ELASTOGENESIS.

H.Länsimies, Dept.of Pathology and Children's Hospital, University of Turku, Turku-Finland.

The purpose of this study was to find out whether the elastogenesis in human ligamentum nuchae resembled that in other mammals described earlier.My material consisted of 25 samples from 29th week of gestation to the age of four years.For TEM study the tissue samples were stained either with lead-citrate,uranyl-acetate or PTA.

The human elastogenesis resembled in general the mammal elastogenesis.Elastic fibers consisted of two elements: microfibril mantle and central amorphous unstaining area.At the early phases of formation the fibroblasts were surrounded by a great number of microfibrils in mucopolysaccharide groundsubstance /28th fetal week/. These microfibrils were identical to the microfibrils in the mantle of the mature fibers. During maturation these fibrils aggregated and"pre-elastic" fiber was formed. Later on the amorphous area /central cord/ was formed and the elastic fiber was mature at about two years of age. The role of fibroblasts is important.At the earliest phases the number of fibroblasts was great and the microfibrils were first observed in their vicinity.The exact role could not,however,be determined at this stage of the study.

HISTOLOGICAL PROBLEMS OF ARTERIAL BYPASS OPERATIONS BY AUTOGENOUS VEIN GRAFTS.

H.J. Leu, U.V.Brunner, Inst.of Path.Anat. der Univ. Zürich-Schwitzerland.

The success of grafting by autogenous veins may be endangered by various kinds of tissue reaction: 1/ Foreign body reaction to suture material is of no great consequence.It is usually restricted to the immediate area of the stitches.This very localized inflammatory reaction does not induce rejection of the graft. - 2/ Infection may set in early or after several weeks of apparently normal functioning.It leads invariably to thrombosis,necrosis and purulent fusion. - 3/ Thrombosis may occur immediately after grafting or may develop slowly and gradually. It may be due to an impaired inflow or run-off in the proximal or distal arterial segment respectively and therefore be due to hemodynamic reasons solely,or it may initiate at wall lesions in the venous grafts.Suture material which penetrated the venous wall at the anastomosis site and which lies intraluminally in direct contact with blood has proved to be not infrequently responsible for this complication. - 4/ Narrowing of venous graft lumen may be due to gradual thickening of the intimal layer. Connective tissue is incorporated in the venous intima. This process is gradually progressing and may cause stenosis of the lumen.It is often complicated by formation of thrombi.It is questionable whether this reaction may be favourably influenced by prolongated anticoagulant treatment. - 5/ Formation of aneurysms in the vein graft may occur.It seems that varicose veins as well as apparently normal veins of subjects suffering from varicose veins are prone to segmental dilatation and should not be used as grafts.

OBSERVATIONS ON THE DYNAMICS OF DNA-METABOLISM OF EXPLANTED VASCULAR WALL CELLS.

P.F.Mahnke, H.Krug, Ch.Bierbaum, Dept.of Cell Cultivation and Cytophotometry,Inst.of Pathology, Karl-Marx-University,Leipzig-GDR.

The examinations sere performed on 800 cells from explants of embryonic chicken aorta. Cell culture technique: cultivation in modified Carrel flasks with two coverslips,in Eagle's and Parker's media with added serum. Culturing was interrupted at different points of time and the explants were stained with Feulgen's technique. /Schiff's reagent, cold hydrolysis for 30 minutes at 20°C, 5 N HCl, staining time 35 minutes./ Absorption was then measured with a cytophotometer of the authors' own construction, which makes possible the continuous recording of extinction. Arbitrary working units were established by planimetry of the extinction curves. The nuclear surface was also measured.

The proportions of diploidic and tetraploidic nuclei were established for each individual cell. The diploidic peak value was at 47 AU, the tetraploidic one at 90 AU. The relationship of the DNA-content /expressed as AU/ with the nuclear volume was checked.

FIBRILLOGENESIS IN RELATION TO ARTERIC LESIONS

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The problem of regeneration of the elastic tissue of arteries has not received much attention. The internal elastic lamina is said to split and re-duplicate while the term fibro-elastosis is used for the finer mixture of elastic tissue and fibrous tissue which appears in the intima and also in the endocardium. Lendrum has recently postulated that the apparently newly formed elastic tissue may be derived from altered fibrin which may first come to stain as collagen (pseudo-collagen) and then further alter in capacity to bind dyes so that it stains with elastic tissue stains in a similar manner to actinic elastosis of the skin. By use of pre-oxidation with oxone it is possible to stain pre-elastic fibres and an attempt has been made to distinguish these from fibrin and collagen by staining methods and by use of photography with blue light fluorescent microscopy. It has not been possible to identify the cells responsible for laying down these fibres, but it is likely that they may be derived from circulating mono-nuclear cells or from wandering so-called smooth muscle cells.

ELASTOGENESIS IN EXPRIMENTAL ENDARTERITIS IN RABBIT.

MM. J. ROLAND et A. ROSNOWSKI

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Changes occuring in exprimentally produced endarteritis of femoral artery in rabbit during several months have been studied. By the mean of a plastic coating around the artery, the animals early showed an intimal proliferation of fibroblast-like cells, subsequantly of muscle cells. Elastic material is seen, produced by the new-formed intimal cells during the first weeks; the elastic units are numerous and a neo-elastic membrane is organised after eighth month in sub-endothelial position, whereas the elastica interna is always present.

The importance of the 'multifunctional mesenchymal cell", in case of injury and repair of arterial wall, and the relation between mesenchymal cell and elastic tissue are emphasized. Organoïd elastogenesis reappearing after fœtal or neonatal periods is demonstrated by this experimental procedure. The conversion of a muscular into musculo-elastic artery is possible and is believed to depend on new circulatory conditions.

POLARIZATION OPTICAL STUDIES.

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2nd Dept.of Pathology of the Semmelweis Medical University,Budapest and Surgery Department of János Hospital,Budapest.

The connective tissue and smooth muscle elements were examined in the experimentally damaged abdominal aortas of dogs.Various staining methods and polarization optical technics were applied to specimens digested by trypsin or pectinase after pretreatment with $KMnO_4$, methylation and oxone-treatment, sulfatation, methylation and sulfatation or methylation and acetylation.

Methylation and oxone-treatment was found to protect for prolonged times the collagenous fibres against the action of trypsin. Pretreatment with $KMnO_4$ facilitated digestion of the argyrophilic- and collagenous fibres and of the smooth muscle cells, while it rendered the elastic fibres somewhat more resistant. Similar results were obtained with prolonged exposure to pectinase. In methylated and sulfatated as well as in methylated and acetylated specimens the elastic and collagenous fibres were digested more readily than the smooth muscle cells. Enzymatic decomposition was the fastest in the necrotic areas of the aortic walls,intermediate and slow effects were observed at the borderline area and in the intact parts of the aortic walls,respectively.

ULTRASTRUCTURAL ASPECT OF ROLE OF SMOOTH MUSCLE CELLS BY ARTERIITIS IN MAN AND ANIMAL

Takebayashi,Sh., Kubota,I., Dept.of Pathology, School of Medicine, Nagasaki University, Nagasaki-Japan.

The proliferating cells in obliterating endoarteriitis of human stomach ulcer and obliterating thromboangiitis of Bürger's disease consisted of the smooth muscle cells. At the acute or fulminant stage,the cell was of increased rough endoplasmic reticulum /rER/ and Golgi apparatus,and of decreased or disappeared myofibril and dense attachment,like a fibroblast.At the chronic stage, however,the cell was of decreased rER and Golgi apparatus, and of reappeared myofibril and dense attachment which was characterized as a smooth muscle cell.At the latter stage /healing stage/ where inflammation disappeared, all proliferated cells appeared as normal smooth muscle cells,and numerous elastic and collagen fibers were deposited in irregularly dilated intercellular spaces. No fibroblast nor fibrocyte was present in any place of the intima or media. The same results were obstained in the processes of experimental periarteriitis nodosa which appeared in the mesenteric arteries of hypertensive rats. It was concluded that the medial smooth muscle cells play a very important role in the processes of arteriitis and the morphologically and functionally they serve as fibroblasts under an inflammatory condition of artery, like in an intimal thickening of arteriosclerosis.

FATE OF AUTOLOGOUS VEIN GRAFTS AND SYNTHETIC PROSTHESES USED FOR REPAIR OF HUMAN ARTERIES

Walton, Kenneth W.

Department of Experimental Pathology, University of Birmingham, England.

Autologous saphenous vein, or tubes composed of teflon or dacron are increasingly used for bypass or replacement of arteries occluded by atherosclerosis. There is controversy about the nature of the pathological changes which occur in such grafts with time. It has been established previously by immunofluorescence that low- and very low-density (beta) lipoproteins transport lipid into atherosclerotic lesions at all stages of their development. Using a similar method, a series of femoro-popliteal grafts removed after being in situ for periods between ½-10 years have been examined. It will be demonstrated that the process of 'arterialization' of vein grafts is accompanied by lipid deposition and that the lipid is identifiable as beta-lipoprotein. Similar changes will be shown to occur in the fibrous tissue which develops around synthetic prostheses. This suggests that, in each instance, a process develops resembling in mechanism that found in the originally affected artery.

THE EFFECT OF COPPER /II/ ON THE CONNECTIVE TISSUE OF THE RAT AORTA.

M.Zlateva, G.Antov, V.Gelabova

Superiour Med.Inst. Várna-Bulgarian.

The authors study the effect of Copper /II/ on the amount of the soluble and insoluble collagen and of the acid and neutral mucopolysaccharides, isolated from rat's aorta after oral administration of 1/20 L D_{50} $CuSO_4$ for 6 mounths. Whilst the amount of alcali--soluble collagen, insoluble collagen, uronic acides, sialic acids and sulfated mucopolysaccharides increase, these of soluble proteins and soluble decrease.

From the investigation it may be concluded that Copper /II/ in toxic doses would cause arteriosclerotic changes and changes in the permeability of the experimental animals aorta.

PATHOLOGICAL PROCESSES OF THE ARTERIES

Invited lecturers

ASTRUP, P., KJELDSEN, K.
HOLLE, G.
KOJIMAHARA, M.
LUSZTIG, G.
MORRISON, L. M., BAJWA, G. S., ERSHOFF, B. H.
ROBERT, L.
ŠOUSTEK, Z.
TEXON, M.
YOSHIDA, Y.

THE EFFECTS OF HYPOXIA RESP. HYPEROXIA ON THE DEVELOPMENT OF ATHEROSCLEROSIS

Astrup, Poul and Kjeldsen, Knud

Department of Clinical Chemistry A Rigshospitalet, Copenhagen, Denmark

Exposure of rabbits, fed or not fed cholesterol, to hypoxia greatly enhanced the development of atherosclerosis, while exposure to hyperoxia had an opposite effect. The results of biochemical, physiological and ultrastructural studies of the involved mechanisms are given, and the significance of the findings for prevention and treatment of atherosclerosis in human beings is given.

DYSMETABOLIC STORAGE LESIONS OF ARTERIAL MEDIA IN HUMAN PATHOLOGY.

A.Batzenschlager, M.Fievez, J.M.Vetter,

Institute d'Anatomie Pathologique du C.H.U.-6 70000-Strasbourg,France et Laboratoire de Morphopathologie, Loverval, Belgique.

Three anatomo-clinical observations are analysed and discussed:

idiopathic oxalosis in a 27 year old male;

primary calcinosis in a 20 year old female;

Fabry's disease in a 46 year old male.

The localisation of the alterations in the different structures of arterial media /connective tissue, elastic tissue, smooth muscle/ lead us to state precisely the part of each component of arterial media in the production of these dysmetabolic lesions.

ARTERIOLAR CHANGES IN POST-RADIOTHERAPEUTIC NECROSIS

Elisabeta David

Oncological Institute,Cluj,Romania

Radionecrosis is a lesion frequently met in oncological practice, several months or even years after the cessation of radiotherapy.

In this sense, the histological and histoenzymochemical changes were studied in 300 operatory pieces removed from patients with radionecrosis.

In all cases, vascular changes characterized by endothelial hyperplasia, diffuse thickening of the arteriolar wall going to a partial or even complete obliteration of the vascular lumen were seen. A diminished activity of the alkaline phosphatase, an obvious activity of the acid phosphatase, limited to the borders of the endothelial hyperplastic cells and associated with a decreased argirophilia of these cells were also observed in most cases.

These vascular changes are followed by degenerative changes of the colagenic and elastic fibres, with marked fibrosis and atrofy of the irradiated tissue, leading to necrosis.

Our data argue for the primordial role of the vascular changes in appearance of post radiotherapeutic necrosis.

IDIOPATHIC AORTITIS IN CHILDREN.REPORT OF TWO CASES.

Ferluga,Dušan and Lamovec,Janez

Institut of Pathology, Ljubljana, Yugoslavia

Idiopathic aortitis is a rare disease with different clinical presentations and different gross and histological appearances, and probably with different etiology as well. Two our cases are presented. First patient was a boy who died 6 years old,and second a 9 year old girl.In the first case the aortic disease developed during the admittance for undefined febrile state, and appeared as isthmic coarctation. The patient has been operated upon and the coarctated part of aorta excised. The histologic examination of the excised aortic tissue revealed granulomatous giant-cell aortitis with massive disruption and fragmentation of elastica. Later on, the patient died during the second of two subsequent operation performed for excision of the huge pseudoaneurysm which appeared at the transplantation site. In the second case the totally asymptomatic aortic changes were found accidentally during the autopsy of the 9 years old girl who died of mucoviscidosis. Histologic examination of the changed aortic tissue revealed nonspecific inflammatory infiltration in the fibrosed media and adventitia with focal disruption and fragmentation of elastic lamellas. The giant-cell granulomas similar to those described above were not found. In discussion different possible etiologic agents are considered, and the point that deep cutaneous Candida infection in both cases was found, is stressed which would suggest the possibility of some kind of hyperergic inflammatory local reaction

THE IMPORTANCE OF DEEP FEMORAL ARTERY - AS A MAIN COLLATERAL - UNDER PATHOLOGICAL CIRCUMSTANCES

Fontányi, Sándor Rakonczay, Gyula and Lauf, László
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As obliteration of superficial femoral artery is more common than that of the deep one, the latter is mostly able to function as the main collateral of the lower extremity. This function may be absent or restricted - and so his importance becomes more distinctly evident - in some pathological conditions /aplasia, hypoplasia, occlusion and stenosis of inflammatory or degenerative origin/.

Arteriography of 7 severe ischemic limbs - out of 300 cases with peripheral vascular occlusion - revealed in 4 instances no function and in 3 cases a severe restriction in function of the deep femoral artery. The simultaneous obliteration of the superficial femoral or the popliteal artery was present in each of the cases. The rapid formation of gangrene was charecteristic after the appearence of the first symptoms, as the development of a collateral network was not possible.

We present brief history, arteriography, macro- and microscopic patterns. We found the absence of the main collateral to be more decisive, than the pathological character of the obliterative disease.

IMMUNOHISTOCHEMICAL FINDINGS IN VESSELS OF THE SYNOVIAL MEMBRANE WITH RHEUMATOID ARTHRITIS

Geiler, Gottfried
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With active rheumatoid arthritis, deposits of immunoglobulins (IgA, IgG, IgM globulins) and complements which can be detected immunohistochemically are to be found in arteries, arterioles and precapillaries of the synovial membrane. Appropriate findings were observed in 10 of 31 synovial membranes. The immunoglobulins are formed by plasma cells which are to be found in great number in the synovial membrane with rheumatoid synovitis. Since the locations of complement binding indicate the presence of antigen-antibody complexes, it can be taken for granted that immunoglobulins found in the same structures also form part of these immunocomplexes. It is assumed that immunocomplexes which are deposited in the vessels induce inflammatory changes of the vessel with rheumatoid arthritis.

CHANGES OF WATER-BINDIG CAPACITY OF HUMAN AORTIC WALL WITH AGING

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Dept. of Pathology County Hospital
Kecskemét, Hungary.

We examine in our present work the changes of water-binding capacity of the aortic wall with aging. Data found in literature only refer to alterations of water-content of the vessel-wall, by our knowledge investigations concerning the water-binding capacity of the wessel-wall were not yet performed.
We made our examinations with the method of ASBOE-HANSEN. Our cases were divided into three age-groups. /20-25, 40-55, 60-75 years/ The results show, that with progression of age, the water-content is decreasing, both of the intima-media and the adventitia. In the intima-media the speed of water-loss is decreasing as well, while in the adventitia the latter is increasing with progression of age. Our observations point to the fact, that in old age the decreased water-content of the wessel-wall becomes more immobilized in the intima-media, while in the adventitia parallel to this, a water-loosening process is taking place. As the chage of water-binding capacity refers to the colloid-structural alterations of the tissue - we consider our observations to be of some interest.

EXPERIMENTALLY-INDUCED EARLY CHANGES IN ARTERIES

by G. Holle
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There still exist controversial opinions on the initial changes in atherosclerosis. Light- and electron-microscopic studies of this problem were carried out in three test series with rabbits. Method: A. Continuous and intermittent cholesterol-rich diet over a period of 12 to 18 weeks (144 animals). B. Immunisation by subcutaneous injections of 3x2 ml of horse serum with subsequent intravenous boosting with 2x3 ml (6 animals). C. Immunisation and subsequent cholesterol-rich diet for 4 to 8 weeks (28 animals). Result: Light-microscopic examination: With exclusive cholesterol-rich diet, proliferation of myointimal cells with high-degree transformation into foam cells in the aorta, no transformation into foam cells in the coronaries. After immunisation, accumulation of myointimal cells and macrophages in the aorta without any essential lipid storing. Additional cholesterol-rich diet produced a pronounced potentiation of the findings. Electron-microscopic examination: After immunisation, signs of raised permeability on the endothelium, damage of elastic material and increased secretory-metabolic activity on the smooth muscle cells. Additional cholesterol-rich diet enhances the findings. Conclusions: The walls of the vessels exhibit only few typical reaction mechanisms and reacts different in different vascular regions.

THE POSSIBLE INTERDEPENDENCE OF CARDIOVASCULAR DEFECTS AND NEURO-CIRCULAR ASTHENIA IN MARFAN SYNDROME

Hollósi,Katalin

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Cardiovascular anomalies, chemo- and baroreceptor lesions were studied by autopsy and histologically in 3 Marfan syndrome cases. A 18 years old man died after the repeated rupture of cerebral aneurysms. Extensive cardiovascular defects, extensive hyperplasia of the glomus coronarium, unequaled in literature, were found. In the case history an unstable hypertension was mentioned. Latter is associated to the hitherto " forme fruste" Marfan syndrome of the patient's sister. It is assumed that the vasa vasorum injury of the aortic arch might have reduced the blood pressure equilibrating function of the baroreceptor reflex. The extreme hyperplasia of the glomus coronarium might have been of compensatory character. In this case the interdependence of the syndrome with cardiovascular defect and the neuro-circular asthenia is plausible. Experiences have shown that beta-receptor blocking agents, the possible use of cardio-selective drugs might prolonge survival in latter case. The importance of referring juveniles suspect of Marfan syndrome to a special departement is emphasized.

ARTERIAL LESIONS IN HUMAN RENAL ALLOGRAFTS

Kalpaktsides-Vakiani,M., Gabrielides, Cl. and Polyzonis, M.

Pathology Departement, Aristotelian University, School of Medicine, Thessaloniki, Greece.

The arterial lesions of 12 human renal allografts, referred to our Departement as whole specimens, were studied. The grafts were donated by living relatives (6), non-relative cadavers (3) and living non-relative (1), and had remained in the recipients for periods of from 40 days to 14 months.

Following the usual histopathological technique of paraffin embedding and the application of special stains arteries of all calibers were blindly studied.

The main (arterial) lesions noted were : 1)multiplication or disruption of the internal elastic lamina and intimal thickening due to the development of often basophilic fibrous tissue 2) thickening of the media of the main branches of the renal arteries which contained many collagen and elastic fibres and contrasted that of the interlobar,arcuate and intralobar arteries whose media was relatively thin 3) thickening of the adventitia due to the development of fibrous and elastic tissue which was abundant and irregular, particularly in the main arteries.

Extensive acute arteritis with thrombosis was noted in the necrotic grafts.

It was found that the function of the grafts was directly related to the severity of the arterial lesions noted.

PRIMARY ARTERITIS OF THE AORTA AND ITS BRANCHES

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In the last two decades numerous reports have appeared in the medical literature describing cases of non specific aortic arteritis. The disease may not be confined to the aortic arch, but could also be located in the thoracic or abdominal segments, and may spread into any of its braches, but does not seem to affect other arteries. Grossly is a localised thickening of the wall, with narrowing of the aorta, or its branches. Microscopically the changes are characterized by marked fibrosis and hyperplasia of the intima, disruption of the elastic fibers in the media, cellular infiltration in the media and adventitia, and marked fibrosis of the adventitia. Aetiology in unknown. Clinical manifestations of the disease depend of the extent and location of the lesions in the aorta or in its branches. Our patient, a 10-year-old gipsy girl, was treated 10 months ago with rheumatic heart disease. She was admitted secondly to our hospital 3 months later with cardiac failare. Her blood pressure was 160/80, Femoral pulses was absent, radial normal. Coarctation of the aorta was supposed. She developed pulmonary oedema and died. Autopsy findings were similar, which have been observed by Isaacson, Danaraj and Wrong. Autopsy and microscopic findings will be demonstrate in detail. It is our thesis that the lesions of the so-called "aortitis syndrome" in our case could represent involvement of the aorta, carotid arteries and pulmonary arterial trunk by rheumatic fever.

KÖHLMEIER-DEGOS DISEASE. CASE REPORT AND NOSOLOGIC DISCUSSION.

Knutson, Hugo

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As originally described, this rare cutaneo-intestinal disease, probably fatal to 100%, starts with characteristic cutaneous lesions followed in months-years by an abdominal catastrophe with gastro-intestinal perforation and peritonitis. In later publications a cutaneo-cerebral syndrome has been added, also fatal but with a more protracted course. In addition, several cases showing only the skin lesions have been reported. The ultimate fate of these patients is not known in spite of observation times up to 14 years.

The pathogenesis of lesions in typical cases is usually presented as a chronic thrombosing peripheral endarteritis of unknown cause. Descriptions often seem to be oddly at variance with the acute clinical course of the intestinal lesions.

An attempt will be made to illustrate the nosologic position of this disease with material from a recently observed case, stressing the occurrence of acute changes, with reference to immunological phenomena.

CHANGE OF CEREBRAL ARTERI IN AGING AND EXPERIMENTAL HYPERTENSIVE RAT STUDIED WITH ELECTRON MICROSCOPE. M.Kojimahara, 2nd Dept. of Pathology, Gunma University, Maebashi-Japan

Anterior cerebral arteries of aging rats /3-20 months of age/ and hypertensive rats /4 weeks-10 months after the constriction of the renal arteries/ were studied. In either group of rats, typical alteration was focal cytoplasmic necrosis of the medial smooth mucle cells /SMC/ in both proximal and branching segments. Around the SMC, which were reduced in size, there were dense granules, vesicles, vacuoles, dense masses, and basement membrane-like substance. These profiles would be products of disposal of necrotic cytoplasm and remained in the media without producing any detectable reaction. In aging rats, the change was striking in the outer media. Degree of the necrotic change in the media was markedly accelerated owing to hypertension. In both broups, fibrosis was observed in the outer media and adventitia. Any marked change was not seen in the intima of the proximal segments.

Intimal pads /"valve"-like projection//IP/ were always found at branching points of the cerebral arteries. The cells in the IP were SMC. The necrotic change of the SMC at branching points in hypertensive rats was far more when compared to those of normal aging rats. Distinct plasma infiltration was seen in the small branches of the cerebral arteries in rats with damaged media and hypertension.

HISTOPATHOLOGICAL CHANGES IN THE ARTERIAL VESSELS OF SPONTANEOUSLY HYPERTENSIVE RATS (SHR)

Laban, Ana; Bata, Antal; Išvaneski, Milorad; Jovanović, Branko and Lastić, Sofija

Institute of Pathology and Institute of Pathological Physiology, Belgrade, Yugoslavia

Investigations were performed on the 22nd and 23rd generations of genetically hypertensive rats (strain Okamoto-Aoki, domesticated in Yugoslavia by Nikodijević), aged 6, 8 and over 12 months.

Hyperplastic arteriolosclerosis has been found in all animals, 25/25. In the group aged over 12 months, besides severe arteriolosclerotic changes, periarteritis nodosa - like lesions have been discovered in 5/5 cases in the medium size and smaller arterial blood vessels. In the 8-month-old group, changes similar to PN have been observed in 5/8 cases; these changes have only been found in 3/12 cases in the 6-month-old group. The lesions are in correlation with the height of systolic pressure, i.e., with the age. Granulomatous changes were located primarily in mesenteric arteries, very rarely in kidneys. In our series, the changes occur in a much higher percentage than it was stated in earlier publications. This allows for a conclusion that in later generations of SHR, vascular lesions appear in a more severe form and in a higher percentage.

ABOUT THE ROLE OF ADVENTITIA IN THE CHANGES OF AORTA INTIMA-MEDIA

Lusztig, G. Dept. of Pathology County Hospital Kecskemét, Hungary.

The results concerning the vascularization of the atherosclerotic aorta-wall are contradictory.

We have established, that changes take place in the artery-system originating from the aorta -in aging. Swelling of the endothelial cells, vascularization and moderate acid-mucopolysaccharide-increase are observed. The lumen-wideness of vasa-vasorum, originating from the branches perforating the aorta, is increasing with proceeding of age. The number of vasa-vasorum does not show any similar changes.

There is a certain connection demonstrable between the number of mast-cells and the dilatation of lumen of vasa-vasorum, inasmuch the number and volume of mast-cells indrease with the progression of age. By my opinion the number and volume of mast-cells increase by the influence of hypoxic changes demonstrable in the artery-system perforating the aorta, which goes together with renewed Heparin and Histamin content.

This creates a milieu, in which the vasa-vasorum, with the dilatation of their lumen, are helping the nutrition of the damaged aortic-wall, from the side of the adventitia.

Consequently, the adventitia restrains pathological processes, taking place in the intima-media, first of all the regressive changes proceeding with aging.

CORRELATIONS BETWEEN LIPID STATUS AND MUSCLE BIOPSY FINDINGS IN VASCULAR DISEASES.

P.F.Mahnke, R.Emmrich, Helga Marek, Alois Ziegler, Brigitte Haaser, Annerose Neugebauer, Inst.of Pathology and Clinic of Internal Diseases, Karl-Marx-University, Leipzig-GDR.

The role of the different types of hyperlipoproteinaemia in the pathogenesis of vascular diseases is still far from clear. Thirty-seven patients with a sure diagnosis of arteriosclerosis, part of whom also had a malignant hypertension were examined for the type of hyperlipoproteinaemia and biopsy specimens from the femoral muscle of each were examined for the state of the arterioles to draw conclusions on a possible correlation. /The electrophoretic methods and type differentiations were carried out according to FREDERICKSON, using the common histologic and histochemical methods. Twenty-four of the patients had hyperlipoproteinaemia and among them 13 had a different degree of arteriosclerosis, to judge from the biopsy specimens. Type 2 seemed to play a role in "young" age and type 4 in advanced age also in the peripheral vessels. The probable role of type 3 is discussed.

ULTRASTRUCTURAL CHANGES OF ARTERIOLAR MEDIA IN THE SKELETAL MUSCLE OF ARTERIOSCLEROTIC PATIENTS.

Mandache,E., Balta,N., Saptefrati,V.
Inst.of Pathology "Victor Babes" and Med. Gen. Bucharest-Romania.

Ten arteriosclerotic patients have been investigated clinically and morphologically. The muscular biopsies have been examined with the electron microscope. Following the blood vessels ultrastructure, we found on 7 patients modifications of the arteriolar media. The lesions are located especially between the muscular layer and the endothelium. The smooth muscular layer is slightly involved in the pathological process. This work presents the aspect and the degree of the above mentioned lesions.

A QUANTITATIVE APPRAISAL OF MÖNCKEBERG ARTERIAL DISEASE IN LOWER LIMB ARTERIES.

Martinazzi, Massimo and Carnevali, Luciano
Institute of Morbid Anatomy, University of Pavia, Italy.

The percentage of people affected by Mönckeberg disease, the number of damaged arteries as a percent of all arteries from each subject and the areas involved (pocket evaginations) as a percent of total arterial areas, were evaluated in lower limb arteries of an autoptic population of both sexes aged 50 or over, using a quantitative method (point counting) for calculations of areas. Mönckeberg disease is very frequent both in males and females (30% of aged people), but in younger decades males show wider damaged areas. An increase with age of positive cases, of affected arteries and of affected areas is evident in males; in females a dramatic increase is found from the sixth to seventh decade. Anterior and posterior tibial arteries are involved in both sexes to a similar degree, whereas males are more prone to develop Mönckeberg disease in femoral arteries. Mönckeberg disease does not produce arterial stenoses, as judged by "Profile Index".

REVERSIBILITY OF ATHERO-ARTERIOSCLEROSIS IN MONKEYS BY MUCOPOLYSACCHARIDES.

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Institute For Arteriosclerosis Research, Loma Linda University School of Medicine, Culver City, California.

Two groups of monkeys (Saimiri sciurea) were examined as to possible regression of coronary and/or aorta atherosclerosis following treatment by the mucopolysaccharide chondroitin sulfate A (CSA). In the first group of squirrel monkeys approximately 2-3 years old with dietetically accelerated atherosclerosis following 9 months of daily subcutaneous CSA injections, the aortas were found entirely free of atherosclerosis as compared to a sub-set of matched control monkeys despite the feeding of a high atherogenic diet. The second group of squirrel monkeys aged approximately 7-8 years received daily subcutaneous injections of CSA for 90 days with normal diet. Necropsy revealed the basal coronary sections to be free of atherosclerosis, with a reduction in severity of other segments of the coronaries and aortas compared to the spontaneous atherosclerosis in the control monkeys.

These experiments in a sub-human primate species suggest that some forms of atherosclerosis may be reversible.

MICROVASCULAR LESIONS IN SYMPATHETIC GANGLIA OF HUMANS BEARING OBSTRUCTIVE PERIPHERAL ARTERIOPATHIES.

MOSCA, Leonardo and SCELSI, Roberto
Dept. of Morbid Anatomy, University of Pavia Italy

Sympathetic ganglia of lumbar chain of patients affected by obstructive peripheral arteriopathies (20 cases up to 40 ys -2 women and 18 males-; 130 from 40 ys on -15w/115m) show: neuronal damage with the same severity and percentage in both groups; microangiopathy progressively worstening with ageing. Hyaline, amorphous, "hemodynamic" cuffing of the microvessels is the commonest alteration, parallelled, to a lesser degree, by inflammatory reactions, fibrosis and proliferative phenomena. Alcaline and acid phosphatase and ATP-ase activities quickly disappear from damaged vessel walls. Hemodynamic and phlogistic lesions undergo fibrosis, this sequence starting only in a few gangliar vessels in young age, and involve more and more districts and ganglia in senility. There is apparently no relationship between gangliar microvessel pathology and arterial lesions in legs.

ON THE PATHOLGGY OF LUNG ARTERIES IN TUBERCULOSIS

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The pathology of lung arteries in advanced fibro-cavitary tuberculosis and of their innervation was studied on 23 post mortem and 15 resection specimens by means of current histological techniques associated with methods for elastic and reticulin fibers. The nervous structures were examined on serial sections by means of Troitsky's silver block impregnation.

Stress is laid upon the arterial wall non-specific, specific and sclerous lesions parallel to the various lesions met with in advanced tuberculosis and their significance in the appearance of the final heart failure of the lethal cases.

The presence of regenerative intima nerve endings in the lung arteries situated in the immediate vicinity of a tuberculous cavity seems to be a morphological argument lending support to the existence of a neuroreflex mechanism that contributes to hypertension in the pulmonary circulation in fibro-cavitary tuberculosis besides arterial stenosis and obliteration due to inflammatory and sclerous processes.

HEPATITIS B ANTIGEN - ANTIBODY IMMUNE COMPLEXES IN PERIARTERITIS NODOSA

Nowosławski,A.,Krawczyński,K., Siusarczyk,J.,Nazarewicz,Teresa and Brzosko,W.J.
Department of Immunopathology and Laboratory of Electron Microscopy State Institute of Hygiene,Warsaw, Poland

Immunofluorescence and histopathology was employed to study tissues obtained at necropsy from 4 patients with clinically diagnosed hepatitis B antigenemia and periarteritis nodosa. Vascular lesions typical for chronic and subacute stage of the disease predominated in all cases. Deposits compatible in composition with hepatitis B antigen /HB Ag/ - antibody immune complexes were detected by immunofluorescence in many of the subacute and all the acute vascular lesions,and in several kidney glomeruli. Some of these deposits showed avidity for guinea pig complement in the immunohistochemical reaction of heterologous complement fixation. From these deposits, immunoglobulins could be usually eluted at acid pH.

These findings strongly suggest pathogenic role of HB Ag - antibody immune complexes in necrotizing angitis and the accompanying focal glomerulonephritis.

FIBRINOID NECROSIS BY VASCULAR LESION INDUCING FACTOR OF KIDNEY EXTRACT

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Fibrinoid necrosis in the small arteries induced by the kidney extract had been thought to be due to the renin and/or renin-like substance(s), increasing the intraluminal pressure and/or permeability.

In this paper, renal cortical extract obtained from normal and renovascular hypertensive rats was fractionated into subcellular fractions by the step-wise centrifugation.

Renin content was the highest in the lysosomal fraction and absent in the microsomal fraction. These two fractions were injected into renoprival rats.

The lysosomal fraction produced severe vascular lesions, pancreas edema and pleural effusion. When large dosis of the microsomal fraction was administrated, it could also produce fibrinoid necrosis in the pancreatic small arteries without blood pressure elevation.

The experiment suggests that the vascular lesion inducing factor other than the pressor factor exists in the microsomal fraction of the kidney extract.

ON ARTERITIS IN POLYMYALGIA ARTERITICA

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Polymyalgia rheumatica sive arteritica is a chronic disease in elderly patients who suffer from general malaise and pains in the shoulder and pelvic girdle and often maximally increased E.S.R. - In 24 patients with this syndrome extensive studies were made of the aorta and large arteries (around 100 transverse sections per case). Typical lesions were circumscribed necroses in the medial coat with chronic inflammation. Multinucleated giant cells were not a constant finding and did not seem to be a prerequisite. (The term "giant cell arteritis" has been used but seems obsolete). - The arteritis differed from the lesions seen in syphilis, medionecrosis aortae and polyarteritis nodosa. In the late stages, morbus Takayasu gives similar changes in the large arteries. - The extent of the lesions was registered in diagrams. Arteritis was seen most often in the aorta, in some cases patchwise but in most continuously. The brachiocephal arteries were engaged more often than the caudal. Frequency analyses were made of arteritis in a 15-year necropsy material from Malmö. 0.4% had arteritic changes. - In a prospective study of aorta and temporal arteries arteritis was found in 1 to 1.7 % of necropsy cases. The disease seems to pass clinically unrecognised in many cases. Complications occurred more often than in syphilitic arteritis.

RECENT INVESTIGATIONS ON THE MECHANISM OF IMMUNO ARTERIAL LESIONS.

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Human sera contain antibodies to soluble elastin. Arteriosclerotic plaques contain immunoglobulins fixed to degrading elastic tissue (immunofluorescent technique and elution of gamma-globulins). It was postulated that autoimmunisation to degrading elastic tissue could be an important factor in the development of arteriosclerosis. Rabbits immunised with arterial extracts (1M $CaCl_2$ extract, structural glycoproteins (SGP) and purified elastin) develop severe arteriosclerotic lesions (70 % of the animals immunised with elastin, about 50 % with SGP and about 10 to 20 % of the animals immunised with diffusible macromolecules). The antigenicity of these substances (passive hemagglutination) varies inversely with their potency to induce arteriosclerosis. Diffusible peptides reacting to anti-elastin antibodies could be demonstrated by immunodiffusion and passive hemagglutination in the $CaCl_2$ extract of aorta. These peptides are degradation products of elastin and may play a role in the process of autoimmunisation as sensitising antigens. Blood platelet elastase may play a role in this degradation process.(Exper. Geront. 5, 339, 1970 ; Eur. J. Biochem. 21, 507, 1971).

VASCULAR CHANGES IN HUMAN ALLOTRANSPLANTED KIDNEYS

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Vascular involvement in human allografted kidneys will be demonstrated with special reference to the obliterative arterio/lo/pathy /OA/. The study is based on 63 clinical biopsies, 12 resected and 13 autopsied transplants examined by optical, electron and immunofluorescence microscopy.-OA exhibits severe stenosis to obliteration of lumen by oedematous, infiltrative and proliferative process, different from usual patterns of arteritis and arterio/lo/sclerosis. Thrombosis is scarce or inapparent at the stages investigated. In ultrastructure, severe degeneration of both muscular and endothelial cells and accumulation of intercellular débris are evident. In major muscular arteries, dystrophic changes involve chiefly the media and deep layers of the intima, while in superficial intimal zone muscular proliferation predominates.- OA is a sign of grave prognosis pointing to actual or imminent graft insufficiency and predicting the necessity of transplantectomy.-The relations of typical OA to "endarteritic" allograft lesions will be also discussed.

ELECTRON MICROSCOPIC OBSERVATIONS OF THE BLOOD VESSELS OF THE PAROTID GLAND IN SJOEGREN'S SYNDROME

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The ultrastructure of myoepithelial sialadenitis ("benign lymphoepithelial lesions", autoimmune sialadenopathy) was investigated in 7 cases of Sjoegren's syndrome. The pathognomonic islands of myoepithelial cells are derived from the intercalated ducts. In later stages there is destruction of duct epithelium, proliferation of the myoepithelium and infiltration by lymphocytes and histiocytes. In the final stage extensive hyaline transformation occurs. Besides myofilaments the myoepithelial cells produce basement-membrane-like sustances that are extruded into the interstitium. The capillaries are surrounded by collagen fibers and hyaline material. Probably the collagen fibers are produced by the pericytes. The pericytes have direct contact to the lymphocytes. The endothelial cells show an extensive swelling of the cytoplasm. The myoepithelial cells and pericytes react in a similar way on immunosuppressive treatment.In the process of dissolution of the intrainsular or pericapillar localizated collagen fibers one finds a direct contact between the pericytes and the endothelial cells. Myoepithelial sialadenitis and the cellular reactions of the blood vessels are regarded as an immunologically induced inflammatory reaction.

THE MUCOUS DYSTROPHY OF THE AORTA AS A CAUSE OF IDIOPATHIC HYPERTROPHY OF THE HEART

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32 cases of the idiopathic hypertrophy of the heart with cardiac insufficiency were analysed.Apart from the histology of myocardium morphological analysis of the aorta was made.

1)The ascending aorta is ectatic;the significant aortic index is established(the relation between the circumference of ascending and descending thoracic aorta).

2)The histology of aorta corresponds to the mucous dystrophy of the media(chronic phase of the Erdheims idiopathic cystic medionecrosis:increased amount of metachromatic mucosubstances and cicatrices).The difference between these changes,atherosclerosis and variant types of aortitis is pointed out.

3)Etiologically the Marfan syndrome is suspected but with minimal symptoms and with aortic manifestation only.

4)The entropometrical studies recommended in Marfan syndrome were done as in the studied group as in patients with acute dissecting aneurysm of the aorta(28cases)as in normal population(120cases).The estimation of metacarpal index from the roentgenogram of the hands is of great importance.

5)The pedigree should be done.The evidence of Marfan syndrome in relatives supports the diagnosis of mucous dystrophy of the aorta.

6)Aortic changes are the cause of heart hypertrophy and represent an inherited mesenchymal disease.

AORTOPATHIES IN UGANDAN AFRICANS

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Twenty-nine cases of non-arteriosclerotic aortic disease seen at autopsy in Ugandan Africans are reviewed. In 17 cases the macroscopic lesions were mainly confined to the proximal part of the aorta which was either thickened or dilated. The majority of these cases had been diagnosed as syphilitic aortitis though the microscopic features and serology only supported this diagnosis in a few cases. In 12 cases the lesions were dominantly in the descending or abdominal aorta and had a focal, segmental or diffuse distribution. All showed localised areas of medial destruction. Four cases presented with ruptured aneurysms, one of syphilitic origin, two mycotic and one due to primary changes in the ground substance. The aetiology of these aortopathies is reviewed and it is concluded that syphilitic aortitis has probably been overdiagnosed in previous reports of cardiac disease in the tropics.

PROTEIN STORAGE, FIBRINOID ALTERATION AND NECROTIZING ANGIITIS IN SLE AND PSS

Szinay Gy.

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1. Qualitatively and quantitatively abnormal se-proteins present in the active phases of SLE and PSS are stored in the RES-cells of various organs, especially in the spleen.

2. The fundamental phenomenon of fibrinoid alteration is always an angiitis localized to capillaries and precapillaries. So the fibrinoid alteration is but another form of necrotizing angiitis.

3. There is a certain parallelism between protein storage, fibrinoid alteration and necrotizing arteriitis, all the three occuring due to abnormal se-proteins.

THE HEMODYNAMIC BASIS OF ARTERIAL LESIONS.

Meyer Texon, New York Univ. Med. Center, Dept. of Forensic Medicine, New York - USA.

Correlated data are adduced from human autopsy specimens, from the laws of fluid mechanics, from hydraulic models, from mathematical /computer/ analysis and from animal experiments in which atherosclerosis was consistently produced by altering vascular configurations in dogs fed a normal diet. The effect of the laws of fluid dynamics is considered the primary factor in the development of atherosclerosis because it alone accounts for the localization and progressive development of atherosclerotic lesions at specific areas of predilection, branching, external attachment, or tapering. Such locations are subject to a local decrease in lateral pressure /tensile stress/ inherent in the local pattern of pulsatile blood flow. Progressive changes range from minimal intimal proliferation to the totally occlusive lesion. Variations in the severity of atherosclerosis are due to differences in local hydraulic specifications, notably blood velocity caliber of lumen and anatomical pattern. For any given blood vessel a normal /physiological/ range of volumetric flow requires a normal range of pressure and velocity which minimizes intimal proliferation due to either excessively high blood velocity or excessively low blood velocity. Intimal proliferation and the progressive development of atherosclerosis are the reactive biological response of the arteries to the mechanical stresses generated by the flowing blood.

ARTERIAL CHANGES IN KALA-AZAR.

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Changes in the vessel wall were detected at autopsy in 12 out of 27 cases of Kala-Azar /visceral leishmaniasis/. These changes affected the small muscular arteries, mainly those of the liver, kidney, heart, bowel and periadrenal tissues. The 12 patients had neither clinically nor at necropsy any signs of hypertension or arteriosclerosis.

The arterial changes consisted essentially of swelling and vacuolation of the lining endothelial cells with accumulation of plasma and hyaline-like material in the subendothelial spaces. No concomittant inflammatory or necrotic changes of the smooth muscle fibres were noted. Two factors are probably involved in the pathogenesis of these arterial changes. a/ The direct effect of the Leishmania Donovani on the endothelial cells resulting in increased permeability and b/the vessel changes may form part of an immunological process. This latter explanation is supported by the finding of atrophy of the lymphoid and splenic follicles as well as by the intercellular deposition of hyaline-like substance in the Malpighian corpuscles and lymphoid follicles. It is hoped that experimental work which is now planned - particularly with reference to histochemistry and electron microscopy - will help to elucidate these observations.

ACID LIPASE AS A FACTOR IN ARTERIAL LESIONS

Wolman, Moshe
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In all storage phenomena, local deposition of any substance results from disturbed relation between ingress (local synthesis and transport to site), and egress (catabolism and transport from site). In most known instances storage is due to deranged egress. It is believed that also in the case of atherosclerosis the emphasis should be on efficiency of the catabolic phenomena rather than on conditions facilitating ingress.

Acid lipase activity has been studied in the aortae of animal species with known different susceptibility to atheromatosis. Aortae of different ages and sites in the arterial system known to differ in their susceptibility to atheromatosis were compared. The results suggest that acid lipase activity plays an important role in atherosclerosis.

PATHOGENESIS OF ARTERIAL CHANGES IN HYPERTENSIVE RATS

YOSHIDA, Yoji
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Arterial lesions in hypertensive rats with bilaterally constricted renal arteries were mainly medial muscle cell necrosis and fibrinoid degeneration. The former preceded the latter. The pathogenesis of medial necrosis is not yet fully clarified. Factors concerning the necrosis were studied. 1. Permeability-increasing substance was extracted from rat kidneys by Asscher & Anson's method. It was injected intraperitoneally into bilaterally nephrectomised rats. The rats were sacrificed at various times after the injection, and their arteries were examined light and electron microscopically. After 3 hrs, slight swelling was noticed in the endothelial cells; blebs were observed in their cytoplasm. Pesin granules used as a tracer for vascular permeability were seen in vacuoles of endothelial cells and the subendothelial space. After 12 hrs, large clear spaces beneath the endothelium and bullae in the cytoplasm of muscle cells appeared. After 18 hrs, disseminated muscle cell necrosis was detected in the media; fibrin deposited in the necrotic muscle cells. 2. The values of Po_2 and pH in blood of the hypertensive rats with constricted renal arteries at 8 weeks postoperatively were lower in rats with prominent fibrinoid degeneration than in rats without it. It is theoretically possible that permeability-increasing factors from the kidney, hypoxidosis and acidosis, besides hypertension, might play some part in the pathogenesis of the muscle necrosis in the hypertensive rats.

ALLERGIC VASOPATHY.

D.D.Zerbino, Med.Inst.,Dept.of Pathology, Lvov, USSR.

Damage to the small vessels in a frequent consequence of both immediate and retarded allergic reactions. The localized as well as the generalized vasopathy represent the effect of the antigen--antibody complex on the vessel wall. We observed vasopathy in collagenosis, obliterative thrombangitis, chronic sepsis and as local or general side effect of drugs.

The term vasopathy coveres a broad variety of histological and histochemical changes such as edema, plasma penetration, fibrinoid transformation, intima proliferation, cellular infiltration, sclerosis and hyalinosis.

The consequences of vasopathy are different in the different organs and have accordingly different effects on the organism as a total. As a result of damaged microcirculation dystrophic and necrobiotic changes occur up to the degree of necrosis or in chronic cases to sclerotic changes.

ARTERIAL LESIONS IN CARDIAC AND RENAL ALLOGRAFTS DURING CHRONIC REJECTION IN RHESUS MONKEYS

Zurcher, C. and Hollander, C.F.
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In order to gain more insight in the mechanisms and morphology of chronic organ rejection and the influence of immunosuppressive treatment on this process orthotopic allogeneic cardiac and renal transplantations were performed in Rhesus (Macaca mulatta) monkeys.

The pathology of chronic rejection in Rhesus monkeys is described with special attention to lesions of the arteries.

The histological features are comparable to those described for man with one exception: no atherosclerotic changes were found in the affected or intact parts of the coronary and renal arteries.

As in man obliterative arteritis appears to be the critical factor in renal and cardiac allograft pathology.

An influence of the immunosuppressive treatment (Imuran i.m. combined with ALS subcutaneously) on the occurrence of this arteritis was not observed.

OTHER PROBLEMS OF CARDIOVASCULAR PATHOLOGY

Invited lecturers

GUSKI, H., BRASELMANN, H., BUNTROCK, P.
THOMASSON, B., LÄNSIMIES, E.
THOMSEN, H. K., KJELDSEN, K.
VELICAN, C.
WIMMER, P., KOZAK, M.
ZERBINO, D. D.

VASCULAR CHANGES IN OPEN-HEART SURGERY

A.Bajtai

Postgraduate Medical School, Department of Pathological Anatomy, Budapest, Hungary

The thrombo-embolic complications and their consequences in several organs of 64 open-heart operated cases are summarised. These changes manifest themselves in different organs but they are most frequent and so most important in the brain. The myocardium, lung, liver and kidney are also affected. In the smaller arteries several kinds of emboli could be found as true fibrin thrombi, antifoam material, bone marrow particle and calcified soils originated from the destroyed heart valves. In the order emboli foreign-body reaction may be found with multinucleated giant cells. The results are disseminated focal or map-like necroses in the brain.

In the myocardium there were infarct-like circumscribed necroses. The wall of smaller arteries were also necrotized in the heart muscle. Platelet-thrombi occured not only in the human material but in experimental circumstances, too. The finding was similar to the disseminated intravascular coagulation in some cases. It may be found e.g. in the lung and kidney. In isolated heart perfusion delicate anoxic change may be found in smaller coronary arteries. Haemorrhagic infarctoid lesion occured in the adrenals.

THE ACTION OF SOME VASOACTIVE DRUGS ON THE MYOCARDIAL BLOOD FLOW IN STATES OF ISCHAEMIA. /AN EXPERIMENTAL STUDY./

N.Dragomir,N.Rottenberg,C.Veleanu,M.Rocsin, Fl.Rottenberg,N.Niculescu,V.Babusceac, Med. School, Timisoara,Romania.

In the paper the action of some vasoactive drugs/lyophylized crataegus extract,spasmochrome,persantine and hydrochloric papaverine/ upon the myocardial microcirculation is investigated in states of experimental acute ischaemia induced by ligature of the left anterior interventricular artery. - In 172 animals /126 rats and 46 dogs/,grouped in 4 sets,doses of the drugs mentioned were inoculated before and after coronary ligature. - The following items have been investigated: EKG, dynamics of SGOT enzymes,coronary blood SGPT, serum and erythrocytar electrolytes Na^+ and K^+, blood flow with 86Rb After sacrification of the animals, micrometer studies were carried out on 11,032 myocardium capillaries.

Based on a comparison of the data obtained with those on controls,the authors state that in the experimental circumstances used, the drugs studied induce a marked improvement of the coronary microcirculation and certain metabolic components in case of acute myocardial infarction/as shown in the diagrams/.The morphological micrometer studies suggest that the action of the drugs is exerted particularly at the "transition region" level situated at the boundary of the ischaemic vs. the irrigated myocardium.

THROMBOSIS OF THE PORTAL VEIN IN NEWBORN INFANTS TREATED WITH TRIS-BUFFER

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1st Institute of Pathology and 1st Department of Gynecology and Obstetrics,Semmelweis Medical University, Budapest, Hungary.

A rapid development has taken place recently in the active medical treatment of disorders occurring in the liquid-electrolyte turnover and acid-base balance of newborn infants. The new therapic methods have, however, involved hitherto not observed complications.

Authors examined the post-mortem material of newborn infants. In 20 per cent of the newborn infants receiving tris-buffer treatment by the cannulation of the umbilical vein, thrombosis was demonstrable in the portal vein. As thrombosis of the umbilical vein occurred only in 5 per cent of their cases, the development of the thrombosis was suggested to be the result of the morphologically demonstrable vein wall damaging effect of the drug and not to the cannulation. In the liver consequential circulatory disorders may occur. On the basis of their findings authors emphasize the importance of following up children treated with the buffer.

INFLUENCE OF LYMPHATIC CIRCULATION ON THE STRUCTURE AND FUNCTION OF THE ISOLATED WORKING RAT HEART

Guski, H., H. Braselmann and P. Buntrock

Institute of Pathology, Humboldt-University Berlin, German Democratic Republic

Because there has been recent interest in the cardiac lymphatic circulation in various pathologic states, the authors have studied the effect of experimentally induced cardiac lymphatic obstruction on morphological and functional conditions of the isolated perfused working rat heart (MORGAN-technique,perfusion with modified Krebs-Henseleit solution at 37°C, measurement of aortic output, coronary flow, pH, and pO_2).

Impairment of cardiac lymph flow has demonstrated by india ink injection into the wall of the left heart after ligation of the lung hili including the pulmonary artery. Histologically, interstitial edema was found most frequently with dilatation of subepicardial lymph vessels. Electron microscopically,there was also some evidence of extracellular and intracellular edema and of damage to heart muscle cells. The experimental findings suggest that impairment of cardiac lymph flow leads to a progressive decrease in the efficiency of the isolated working heart.

ULTRASTRUCTURAL CHANGES IN MYOCARDIUM DURING CONSERVATION OF ISOLATED HEART

Kobidze T.S.
Institut of Experimental Morphology, Department of Cytology, Tbilisi, USSR

Experiments on 24 dogs were performed with the aim of revealing in the myocardium minute submicroscopic changes developed during the conservation of the isolated heart.

The heart conservation has been achieved through coronary perfusion by using the artificial blood circulation apparatus.

The experimental animals were divided into two groups. The animals hearts of group I were perfused with Ringer Lock's solution while the hearts of animals of group II were given a somewhat modified solution of Tirode.

The study of the ultrastructure of the myocardium has shown that the animals subjected to one-hour perfusion developed heavy destructive changes of the cells whereas the animals of group II failed to show any essential marks of change during the same period of time.

EXAMINATION OF CONNECTIONS OF CORONARY ARTERIES WITH POSTMORTEM ANGIOGRAPHY IN HYPOXIC DISEASES.

Leszpyák, J., Dept. of Pathology, County Hosp. Kecskemét-Hungary.

We have demonstrated in our earlier examinations by aid of postmortem angiography, that in every disease, which may cause trouble in the oxygen-supply of the myocard, there are developed apparent connections between the branches of the left and right coronary artery. We have found the majority and most significant connections in chronic pulmonary emphysema. The anastomoses were primarily septal demonstrable, occasionally in the fore wall too. In our present work we proved with similar technique connections to exist, getting X-ray contrast-material not into the chief branches, but in the secondary ones, and were able to demonstrate connections in the above mentioned diseases between the branch-system of the two coronary arteries in the backwall, and around the vena cava superior between the atria-branches. These last communications are especially frequent. The greatest quantity and largest anastomoses were found this time too in case of severe pulmonary emphysems. We demonstrated the same time, that branches, supplying the wall of the left atria are running along the left vena pulmonalis into the hilus and may form occasionally connections with the bronchial arteries. We completed our work with histological examinations, where we have studied the vessel walls, forming connections.

PATHOLOGICAL CHANGES OF THE MYOCARDIUM CAUSED BY X-RAY THERAPY OF THE CHEST AND THE MEDIASTINUM

Éva Magyar, A.Talerman, and R.E.Treurniet,
Postgraduate Medical School, Department of Pathological Anatomy, Budapest, Hungary, and Dr.Daniel den Hoed Kliniek, Rotterdam, The Netherlands

The myocardial changes of 15 patients treated by irradiation because of different tumours of the chest-wall, the lungs and the mediastinum were examined.
The X-ray dosis used varied from 1200 to 6150 R.
The abnormalities found in the myocardium consisted of damages of the small intramyocardial blood-vessels, such as fibrinoid necrosis and proliferative endarteritis. A progressive, diffuse interstitial fibrosis was also present. The parenchyma showed marked degenerative changes and signs of chronic hypoxaemia.
The vascular changes were considered to be primary, and the others as consecutive lesions, caused by the progressive vascular alterations.

INTRAUTERINE LIGATION OF THE LEFT PULMONARY ARTERY IN THE RABBIT.

B.Thomasson, K.Hansinien, Cardiorespiratory Research Unit and Section of Pediatric Surgery, University of Turku, Turku-Finland.

Fetal surgery of the pulmonary vessels in the rabbit is presented in this scientific film /16 mm, seven minutes, in color/.

This method permits extensive possibilities to antenatal modification and experimentation of the great vessels and the heart. Successful studies have been started using the operative methods described in this motion picture.

THE EFFECTS OF CARBON MONOXIDE ON MYOCARDIUM. ULTRASTRUCTURAL CHANGES IN RABBITS AFTER A MODERATE, CHRONIC EXPOSURE.

Thomsen, Henrik Klem and Kjeldsen, Knud

Department of Clinical Chemistry A Rigshospitalet, Copenhagen, Denmark.

Rabbits were exposed to 180 ppm carbon monoxide for two weeks. Focal degenerative changes and necrotised areas were found in the myocytes of the left ventricle.

It is proposed that carbon monoxide in tobacco smoke is an important factor in the development of disperse myocardial fibrosis and may be responsible for the increased risk of myocardial infarction and sudden death seen in heavy smokers.

MORPHOLOGICAL CHANGES IN AORTIC VALVE XENOGRAFTS PLACED IN THE HUMAN MITRAL ANNULUS

Tőszegi, Anna; Csapó, Zsolt; Ormos, Jenő and Kovács, Gábor

Department of Pathology and First Surgical Clinic, University of Medicine, Szeged, Hungary

Stented porcine aortic valve xenografts pretreated with acid formaline were used for the replacement of human mitral valves. Five grafts had to be removed 1-3 years after implantation because of gross regurgitation. Detachment of the aortic wall from the frame was responsible for the failure in all five grafts. Light- and electron microscopy revealed homogenous eosinophilic and amorphous looking material in the cusps and the ring of the aortic wall as a result of degeneration of collagen. Donor cells were no longer discernible but new fibrotic tissue and neointima covered most of the surfaces. Elastica was preserved partly, but fragmented in all grafts. Numerous plasma cells and lymphocytes found at several sites of the cellular infiltration in the grafts were considered as signs of an immune reaction.

COMPARATIVE STUDY ON THE STRUCTURAL ORGANIZATION OF CORONARY AND RADIAL ARTERIES.

Velican, C., Inst. of Internal Medicine, Bucharest-Romania.

A comparative analysis was carried out on the structural organization of 20 coronary/radial artery couples /lesion-free specimens/, exhibiting the same diameter between 2.0 and 1.5 mm and belonging to the same subject. The results demonstrate:

1/ A mean intimal thickness /in um/ of 475 ± 43 for the coronary arteries and 55 ± 18 for the radial ones. A mean medial thickness of 327 ± 39 for the coronary arteries and 692 ± 58 for the radial ones.

2/ The intimal ground substance of the coronary arteries exhibited, as compared to the intimal ground substance of the radial arteries: higher isoelectric point; more intense toluidine blue staining following forced metachromasia and short proteolytic digestions; more abundant material susceptible to both testicular hyaluronidase and sialidase digestion and less abundant substratum susceptible to bacterial hyaluronidase digestion; total reversibility of the methylation blockade following saponification; increased susceptibility to electrostatic and covalent bond-breaking agents.

INFLUENCING OF ARTERIOVENOUS ILLNESSES

Wimmer, Fric, Kozák, Martinek

Scientific department TAD, Cuxhaven

193 patients with arteriovenous disorders of blood supply being administered 1-piperidino-2-methyl-3-p-tolyl-propan-3-one, 3x daily as dragees, 1-2 á 100 mg or daily 1 ampoule i.m., i.v., i.a. á 100 mg. The period of treatment being between 7 days and 4 months. It was caused a lenghtening of the walking distance, an acceleration of the capillary filling, a retardation of the claudication pains, a quicker regulation of the cutaneous temperature, an improvement of the oscillogram, a magnification of the electromyographical activity and an improved amplitude at the plethysmography with regard to arterial disorders of blood supply. The venoustonus being increased, oedema at arms and legs being decreased clearly, ulcera crura being cured at venous disorders of blood supply. A slight hypotonia was partly observed, the renal blood supply decreased a little. Liver- and kidney function as well as the reaction of blood sedimentation were umprejediced.

161 of 173 patients with arterial and venous peripheral disorders of blood supply showed a demonstrable increase of the peripheral hemodynamics. The paradoxical central caused, simultaneous increase of the venous hemodynamics with the arterial hemodynamics may be only explained by an activation of the muscular pump.

RHEUMATOID ARTHRITIS: ELECTRONMICROSCOPY OF CAPILLARIES.

D.D.Zerbino, Med.Inst.Dept.of Pathology, Lvov, USSR.

Biopsy specimens were obtained at surgery of the knee, ankle and finger articulations of patients with infections, non specific polyarthritis. Examinations were performed by light- and electron microscopy. The age of the patients ranged from 24 to 72 years. By electronmicroscopy definite changes were observed in the capillaries. The inner cytoplasmic membrane of the endothelial cells exhibited the formation of cytoplasmic processes and microvilli. Some of the latters were vacuolized and microclasmatotic. A considerable thickening of the basal membrane was found in the capillaries. The elements of the arteriolar wall were distended by plasma inbibition and the pericytes were pushed aside. The arterioles and the capillaries were surrounded by a peculiar, homogenous coat. This was found to be a local phenomenon. In the initial phase of rheumatoid arthritis the permeability of arterioles and capillaries increased while in later phases it decreased considerably. This leads to a chronic hy oxia of the tissues resulting in dystrophy and inflammation and ultimately in sclerosis.

MODERN METHODS IN ELECTRON MICROSCOPY.

Electron histo- and cytochemistry, autoradiography, immuno-electron microscopy, tracer technique, problems of preparation, etc.

Organized by

HÜBNER, G.

Invited lecturers

ADNET, J. J., HOPFNER, C., PLUOT, M., CAULET, T.
AGOSTINI, A.
BOUTEILLE, M.
DUPUY-COIN, A. M., BOUTEILLE, M.
LANGER, K. H., THOENES, W.
MARALDI, N. M., SIMONI, O., BRAGAGLIA, M. M.
REALE, E.
ROHR, H. P.
SHAKHLAMOV, V.
SITTE, H.
SUGÁR, J., CSUKA, O.

ELECTRON MICROSCOPIC DEMONSTRATION OF HYDROLYTIC ENZYMES DURING PATHOLOGIC CHANGES IN CONNECTIVE TISSUE.

Adnet,J.J., Hopfner,C., Pluot,M., Caulet,T.
Lab.Anat-Path.Fac.Médecine, Reims-France.

The authors present two methods for the demonstration of hydrolytic enzymes. The first concern acid phosphatase with a procedure derived from Gomori method, the second concern leucine amino-peptidases demonstrated with a technique based on Nachlas' principle. For the demonstration of amino-peptidase activity, the substrate contains L-Leucy-4-metoxy B Naphtyl amid and the resulting azo dye is chelated by lead salt.

Two applications are presented: one in the Arthus inflammatory process in Hamster cheek pouch, the second in human pseudoxanthoma elasticum.

Enzymatic activity is detected in extracellular space. Control sections were done. The role of these enzymes and the specificity of the reactions are discussed.

APPLICATION AND PROBLEMS OF NEGATIVE STAINING IN ELECTRON CYTOCHEMISTRY AND IN PATHOLOGY

Agostini, Bruno
Max-Planck-Institute for Medical Research, Heidelberg, Federal Republic of Germany

Negative staining has proven a very suitable technique for studying the structure of various biological membranes and plasma lipoproteins under various experimental and pathophysiological conditions. However, certain information on the membrane localisation of enzymic activities have been obtained only by correlative structural and biochemical studies. Structural studies alone cannot be satisfactory, as the stain applied -phosphotungstate, uranyl or molybdate- can interact to a various extent with the membrane lipoprotein, so that the cytochemical patterns obtained depend on the technique applied. Similar behaviour has also been observed on fragmented sarcotubular membranes after delipidation by phospholipase or removal of about 40% protein by trypsin. The stain applied -especially phosphotungstate- can also interact with the product of the cytochemical reaction -Ca or Pb deposits- by bindingions. Negative stains damage in various degree the membrane of catecholamine storage vesicles causing outflow of the vesicular content. Uranyl is the least effective. Appropriate structural analysis of plasma lipoprotein particles can be done when negative staining is combined with enzymic degradation with phospholipase and correlated with results of immunology and X-ray diffraction.

APPLICATION OF HIGH RESOLUTION AUTORADIOGRAPHY AND IMMUNOCYTOCHEMISTRY TO PROBLEMS OF PATHOLOGY

Bouteille, Michel
Inst.Rech.Cancer, 94-Villejuif, France. and UER des Cordeliers, Paris, France.

For the pathologist, the main difficulty is the sampling, which has to be achieved by slicing (liver), cell isolation (spleen liver...) or cell subfractions (isolated nuclei, etc...). The labelling with tritiated precursors is carried out in vitro, and pulse-chase experiments can be performed. After appropriate fixation the immunoperoxidase method can be used on the samples previously incubated with the ^{3}H-precursors, in order to obtain a double labelling (immunocytochemical and autoradiographic) in the same individual cells. For these techniques, coating with emulsion is better made onto single grids, and the advised development method is to combine gold latensification and Phenidon developer, which provide high sensitivity and reproducibility.

A MODIFIED OsO_4 FIXATIVE WHICH SELECTIVELY CONTRASTS MEMBRANES AND GLYCOGEN.

W.C. de Bruijn and P. den Breejen

Department of E.M., Pathol. Lab. Erasmus Univers. of Rotterdam, P.O.Box 1738, Rotterdam, Holland.

The application to aldehyde-fixed tissues of the classical 1% OsO_4 fixative, being modified by the addition of 0.05 M $K_3Fe(CN)_6$, results in selectively contrasted glycogen and membranes in untreated ultrathin sections. The ribosomes are not contrasted. Contrasted glycogen and membranes were also obtained by the addition of $K_4Fe(CN)_6$, or $K_2Ru(CN)_6$, or $K_4Os(CN)_6$ and $K_3Co(CN)_6$ to the 1% OsO_4 fixative, whereas other complex cyanides failed to produce this selective contrast. In addition to the usually observed α- and β-particles, a third non-particulate glycogen is revealed by this method. Acetylation of the aldehyde-fixed tissue cubes and Diastase treatment are used to demonstrate that the contrasted particles are glycogen. Arguments will be presented that the contrast giving complex is composed of hexavalent osmate and $K_4Fe(CN)_6$ which, at high pH, are able to perform: 1).a selective reaction with the tissue ligands present in the membranes and the glycogen, and 2).a complex-forming reaction, such that heavy metal is accumulated at these sites. By the application of blocking reactions to the aldehyde-fixed tissue cubes it will be shown, that the ligand present in the glycogen can be identified as hydroxylic groups, whereas the ligands in the membranes can be identified as aldehydes or ketones. It will be attempted to illucidate the reaction mechanisms involved in this contrasting reaction.

LIMITS AND POSSIBILITIES OF ULTRASTRUCTURAL TECHNIQUES IN THE STUDY OF THE ERYTHROCYTE MEMBRANE. Lucia Câmpeanu and M.D.Ionescu, The Center of Hematology and the Dr.I.Cantacuzino Institute of Bucharest, R.S.Romania.

In the studies performed with ultrastructural techniques on the erythrocyte membrane satisfactory results were obtained with the following techniques: 1). sectioning of the intact erythrocyte embedded in Westophal or in Epon; 2). preparation of erythrocyte ghosts that were examined in two ways: a) - freshly suspended in TRIS solution and directly examined after negative staining on a grid, and b) - after imbedding in Westophal of the ghost suspension and examination after sectioning. Satisfactory photographic reproductions were obtained with these techniques and alterations of the erythrocyte membrane were noted in several diseases such as thalassemia, paroxysmal nocturnal hemoglobinuria, as well as in membranes of stored erythrocytes.

HIGH RESOLUTION CYTOCHEMISTRY AND AUTORADIOGRAPHY OF THE CELL NUCLEUS IN PATHOLOGY.
Dupuy-Coin, Anne-Marie, and Bouteille, M. Inst.Rech.Cancer, 94-Villejuif, France, and UER des Cordeliers, Paris, France.

When a new cell organelle or inclusion is to be investigated by means of the techniques in hand of electron microscopists, the fixation of the pathological sample has to be considered first: aldehyde, non osmicated material is needed. Part of the sample must be embedded in water-soluble plastic (GMA, HPMA...) in order to carry out enzymatic digestions with pronase, RNase and DNase. Selective staining procedures such as the EDTA methods, and more recently intoduced Feulgen-like techniques may also be used. The use of electron-microscope autoradiography requires either special sampling procedures, or an experimental system. In any case, statistical methods such as the density distribution (Salpeter et al.1969) are necessary. The combination of all these methods on some intranuclear inclusions has proved to be possible and informative.

STEREOLOGICAL PROBLEMS IN ULTRASTRUCTURAL MORPHOMETRY

Fritsch, Siegfried

Akademie der Wissenschaften der DDR, Forschungszentrum für Molekularbiologie und Medizin, Zentralinstitut für Mikrobiologie und Experimentelle Therapie, Abteilung Experimentelle Pathologie, Jena, DDR

In submicroscopic dimensions volumetric, surface and numerical analyses can be performed by point counting and integration methods. Regarding the application of these methods to biological objects the following problems will be discussed:

Spatial distribution of substructures (e. g. cell organelles) in the evaluation of their frequency and volume fractions (V_v) and

sampling peculiarities in the evaluation of surface densities (S_v).

Stereometrical results of cells and organelles serve as examples of these problems and provide a basis for dynamic interpretations in functional morphology.

HEPATOCYTE MICROBODIES FOLLOWING LONG TERM TREATMENT WITH CHOLESTEROL LOWERING AGENTS IN DOGS AND RATS.
Hodel, Christian
SANDOZ LTD, Biological and Medical Research Division, Basel, Switzerland

Adult Beagles and albino rats were medicated for 26 weeks with Clofibrate and a phenyl-piperidin derivate, XP 18-975. In appropriate dosage both compounds showed a marked decrease in serum free fatty acids and cholesterol. Very high doses led to signs of hepatotoxicity After killing livers were fixed for histological and electron-microscopical examination. The DAB-reaction was performed on blocks prefixed with glutaraldehyde. The number of microbodies was then counted in semithin sections simultaneously on a projection screen and in the Classimat (automatic visual recorder).

Clofibrate produced in both species, a marked numerical increase in microbodies, with only slightly enlarged hepatocytes. XP 18-975 led to a numerical decrease in microbodies in swollen hepatocytes. Electron microscopy revealed that the average greatest diameter of microbodies after the phenyl-piperidin was significantly raised. The total volume of microbodies was therefore the same per cell after both drugs, whereas the surface area was greatly increased after Clofibrate.

Since both drugs produce marked enzyme induction in the liver, the change in microbody population could indicate that these organelles play an important role in drug metabolism or in drug-induced metabolic changes.

STUDIES ON TRAUMATIC MUSCLE LESIONS OF RATS BY ELECTRON MICROSCOPY AND ELECTRON MICROSCOPIC HISTOCHEMISTRY.

L.Józsa, Dept.of Pathology, State Institute of Traumatology, Budapest-Hungary.

Traumatic injury results in partly focal, partly diffuse swelling of the mitochondria and lysis of the cristae. The increase of the mitochondrial volume was 30% after 30 minutes and 70 and 86% after 60 and 120 minutes, respectively. Defects of the membrane and lysis of the cristae were still seen after 4 and 24 hours, but no swelling was any longer present. Simultaneously with the swelling, the mitochondrial succinine dehydrogenase and lactate dehydrogenase activities fell. The sarcoplasmic reticulum showed different degrees of dilatation, especially in the area of the subsarcolemmal cistern. The fibrils of the myofilaments became lysed in minor areas,but the sarcolemma did not change.

MUSCLE DAMAGES IN RATS ON THE EFFECT OF IMMUNOGLOBULINS

Kelemen, Gabriella and Korényi-Both, A.

Group of Biochemistry, Eötvös Lóránd University and 1st Institute of Pathology, Semmelweis Medical University, Budapest, Hungary.

An experimental model was designed by authors for studying immuno-myopathy by means of immunoglobulins produced against various contractile muscle elements. They examined the fine structural features of immuno-myopathy. The damages were found to involve all organelles of the muscle fibres, and observed to increase in severity with the progression of the time of the experiment.

It is suggested that pathomorphological methods are also suitable for examining some phenomena occurring in experimentally produced immuno-myopathies.

THE ULTRASTRUCTURE OF THE PARTIALLY DIGESTED ELASTIC TISSUE.

Korényi,T.,Bush Valerie, Gardner,D.L., Tádár Anna, 2nd Dept.of Pathology of the Semmelweis Medical University,Budapest-Hungary and The Kennedy Institute of Rheumatology, London-England.

Ultrathin sections of Durcupan ACM embedded chick embryo aorta, rat embryo aorta and adult rat aorta were digested by elastase. Five to sixty minutes of digestion revealed an uranylacetate-lead citrate /UA-LC/ stainable dense granular substructure in the otherwise homogeneous elastic fibers. These granules became faint slowly on prolonged exposure to elastase, but disappeared quickly after a short Tripsin digestion following a five to sixty minutes elastase treatment. The appearance of the granules may represent eitzer the granular structure of the elastin itself or may be the result of demascation of the elastic granules and filaments masked by elastin during the maturation of the elastic fibers. These and other possibilities will be discussed.

FREEZE-ETCH STUDIES ON HUMAN SKELETAL MUSCLE IN THE PATHOLOGICAL STATE.

Ketelsen, Uwe-Peter

Department of Pediatrics, University of Freiburg, Federal Republic of Germany

As the traditional electronmicroscopical methods of preparation usually yield cross sections of membranes, it remained uncertain whether the intracellular reactions in numerous cases of myopathies might not be associated with changes of the macromolecular structure of the muscle cell membranes (e.g. plasma membrane).The freeze-etch method permits the electronmicroscopic observation of membrane faces. With this method changes in the number of internal membrane particles were demonstrated in muscle cell membranes (plasma membranes) obtained from human patients suffering from steroid myopathy. Normal controls of human muscle cells were included. We interprete these findings as a change of membrane structure possibly representing a first step of degeneration of the skeletal muscle cell. Experiments with steroid treated rabbits support this hypothesis.

TRACER PROTEIN-STUDIES ON PERMEABILITY IN THE KIDNEY.

Langer,K.H., Thoenes,W., Inst.f.Cytopathol. d.Universität, Marburg-GFR.

ELECTRON MICROSCOPE AUTORADIOGRAPHY ON THE REACTIVITY OF CELLS CULTURED IN VITRO TREATED WITH ANTIMITOTIC DRUGS

Maraldi,Nadir M., Simoni,Paolo.and Biagini, Graziella.

Istituto di Microscopia elettronica clinica, Bologna, Italy.

The Vinca's alkaloid vinblastine sulfate (VLB) is extensively used as antimitotic in many human neoplasies, owing to its denaturating properties on the spindle apparatus.
Some ultrastructural aspects of cell reactivity to this drug (formation of microtubule crystals and of complexes between microtubules and regular polysomes) are not completely understood (Krishan and Hsu, 1971).
In order to investigate the origin of these structures, white cells from peripheral blood and immature lymphocytes from the thoracic duct have been incubated in presence of Leucine-^{3}H, before treatment with VLB. The dynamic of their formation has been studied by means of electron microscope autoradiography, using a new type of nuclear emulsion (Sakura NR H2), which allows to obtain a very high resolution power.

Krishan and Hsu, J.Cell Biol., 49,927 (1971).

ELECTRON MICROSCOPIC STUDY ON ADRENAL CORTICAL HEMORRHAGE IN INFECTIONS

Mäusle, Ewald
Institute of Pathology, University of Saarland, Homburg, Germany

Suspensions of Salmonella typhimurium, Shigella dysenteriae and Botulinum-A-toxin resp. are injected to 132 male Wistar rats. The basal function of the adrenal is altered by 2 I.U./100 g ACTH and 5 x 0,02 mg/100 g dexamethason resp. in 32 animals each. Glutaraldehyde-OsO4-fixation. Araldite embedding. Zeiss EM 9 S2.

Both endotoxins rapidly cause aggregation of thrombocytes and formation of fibrin, release of monocytes into the blood, disturbance of permeability of the capillary wall with interstitial edema and interstitial fibrin deposits. Lesions of cortical cells and endothelial cells are not visible. Intracortical hemorrhage 14 hours after injection of toxins is regarded as the result of consumption-coagulopathia. The functional state of the cortical cells has no influence on the hemorrhage.

Botulinum-A-toxin does not lead to early alteration of thrombocytes. Platelet aggregation appears first after 14 hours. With Botulinum-A-toxin hemorrhage in the adrenal cortex can be produced only, if at the same time the RHS is blocked. In our study this was done by a dexamethason induced regressive transformation of the adrenal cortex.

ELECTRONMICROSCOPIC CHANGES IN HEPATOCYTES AFTER INJECTION OF METHYLPREDNISOLONE /MP/.

Michaelis,W.E.,Ketelsen,U.,Schneider,M., Dept.of Surgery and Dept.of Pediatric of the University of Freiburg, Freiburg-GFR.

There have been reports on liver changes after application of short acting corticosteroides and communications what belongs to subcellular destructions in the skeletal muscle after injection of MP. 50 SPF-rabbits with an average weight of 2000 gms were formed in 2 groups of 21 animals and treated with 1. one i.m.injection of 60 mgms MP and 2. with 1 injection of the corresponding dose of venicle substance. 8 animals remained untreated.In the usual method light and electronmicroscopic specimen of the liver were made from day 3 to day 60. Beginning from day 3 an increasing depletion of liver glycogen and an increasing fatty degeneration of hepatocytes was found. In the same time an alteration of the rER is seen.We find a splitting of the double membrane of the rER with detatchment of ribosomes and aggregation. This change seems to go over in myelinic degeneration.Similar changes we find in the mitochondrial double membrane besides swelling of the cristae.These alterations often goes over in calcification of the mitos and liver lobules.The maximal alteration we found about day 40 and they decreased until day 60. These experiments show severe damage of the hepatocytes after injection of 30 mgms MP/kg in rabbits. We feare, thet similar changes will be found in infants.

LIMITS OF ELECTRONMICROSCOPIC EXAMINATION ON THE FIXED-TISSUES FOR HISTOPATHOLOGICAL ANALYSIS

P. Nicolescu and Violeta Ionescu
"Victor Babeş" Institute of pathology and medical genetics, Bucharest, Romania

Ultrastructural observations of liver and skeletal muscle rats fragments fixed in buffered-formalin at pH 7, Carnoy and Susa-Heidenhain fixatives, according with histopathological methods, are presented. The fragments were post-fixed in OsO_4 and embebed in epon.

In comparison with specimens fixed and embebed with the usual methods for electron microscopy, there were observed many nuclear and cytoplasmic artefacts. The peculiar artefacts were observed in Susa-fixed specimens and the best preservation of ultrastructure in formalin-fixed specimens.

QUANTITATIVE EVALUATION OF RARELY OCCURRING CYTOPLASMIC STRUCTURES IN ELECTRON MICROSCOPY

Pfeifer, Ulrich
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The number of micrographs needed for the quantification of cytoplasmic structures can exceed a practicable size, if rarely occurring structures are to be evaluated, for example autophagic vacuoles (AV) in parenchymal cells of untreated animals. To overcome this difficulty large areas of tissue are examined directly on the EM screen using the quadratic holes of the specimen supporting copper grids as units of area. A point lattice printed on the screen allows to determine the relative area covered by cytoplasm. The results expressed as AV/µ cytoplasm can be combined with morphometric data obtained by the conventional method. In this way the ratio can be calculated between free organelles (for example mitochondria) and those segregated within AV. This ratio is important when considering kinetics of the turnover of cell organelles and discriminative mechanisms in cellular autophagy.

ULTRASTRUCTURAL DISTRIBUTIÓN OF CALCIUM IN SMOOTH MUSCLE.

Popescu, Laurentiu-Mircea, Ionescu, Nicolae, Stefles, Dumitru, and Dumitrescu, Ioan.
Department of Histology, Faculty of Medicine Bucharest - Romania.

Ultrastructural distribution of calcium in some types of smooth muscle (guinea pig taenia coli, myometrium) was studied by using three methods : two precipitation methods (with potassium oxalate, and potassium pyroantimonate), and a substitution method (with lead acetate).
The results obtained with the three techniques are similary, but complementary in details. The main calcium-storage sites in smooth muscle cells seem to be sarcolemma, subsarcolemmal micro-vesicles, sarcoplasmic reticulum, mitochondria and nucleus.

FIXATION WITH ALDEHYDES.

Reale, E., Anat. Inst. d. Med. Hochschule, Hannover-GFR.

APPLICATION AND PROBLEMS OF QUANTITATIVE ELECTRON MICROSCOPY.

Rohr,H., Inst.of Pathology, Basel-Switzerland.

Experience has shown that automatic morphological analysis is not only difficult but may even be impossible. For these reasons the eye will still play a central role for a long time to come in morphometric analysis. An appliance is now available for the simplification of numerical procedures which arise during morphometric analysis. It is so constructed as to allow the determination of the three basic parameters /volume density, surface density, numerical density/ thusly providing a rational and time-saving method for the evaluation of random samples.
The principle consists of liear grids transmitting electricitiy. Volume determination is done with a special counting pencil which is used to draw cords through the relevant cell or tissue structures. In order to determine the surface area, the pencil is drawn around the structures under analysis, whereby each contact with a grid line results in a recordable impulse. Finally, the number of particles can be simply determined by touching the structures in question. The appliance is provided with an electronic counter which garuantèes high speed numerical work.Various additional extra appliances can be built on,to the basic system.This than allows the instrument to be operated for both light and electron microscopic morphometry.

THE USE OF ELECTRON OPAQUE MARKERS FOR THE STUDY OF PERMEABILITI OF CELLULAR MEMBRANES UNDER NORMAL AND PATHOLOGICAL CONDITIONS.

Shakhlamov,V., Inst.of Human Morph. Moscow-USSR.

INTEREST OF STEREOLOGICAL METHODS FOR THE ULTRASTRUCTURAL STUDY OF HEMOPOIETIC AND IMMUNOCOMPETENT CELLS

Simar, Léon, Betz, Emile, and Weibel Ewald
Institute of Pathology, Liège, Belgium
Institute of Anatomy, Bern, Switzerland

If the qualitative changes of the organelles can be investigated by a normal study with the electron microscope, their quantitative modifications are not detected by these techniques. However, in some physiological and pathological states, the variations of the different components of hemopoietic or immunocompetent cells are essentially quantitative. The ability of the stereological techniques is to detect the quantitative changes which occur in these cells.

In addition to the usual problems inherent to the use of these techniques, three major difficulties appear when studying this kind of cells. The first one concerns the sampling, the second one the estimation of the cell volume from the pictures of the ultrathin sections and the third one is related to the determination of the ribosome content. These different problems are illustrated with an example : the stereological study of the differentiation of lymphnode immunoblasts during the development of the humoral immunity. A semi-automatic technique permits to record the primary data on electrical counters, to transfer them on punch cards and to calculate the different parameters by computer.

PREPARATION OF SEMITHIN AND ULTRATHIN SECTIONS AT NORMAL AND LOW TEMPERATURES

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The present state may be demonstrated by two examples: Comparative light- and electron-microscopy and cryo-ultramicrotomy. Comparative studies are needed, if rare details have to be analyzed. Uniform fixation is a condition, which is achieved by using flat specimens or perfusion. Semithin sections (STS) of large areas allow LM-preexamination followed by controlled trimming and ultrathin sectioning. Since the aspect rapidly changes from one STS to the next, the last STS should be compared with the first ultrathin sections (UTS). STS should as thin as possible. Trimming is done by a special device under LM-control. The use of a diamondknife is preferable (sectioning of hard materials, lower thickness and distortion of UTS).- Cryoultramicrotomy has opened new possibilities in cytochemistry, control of methods and speed, although it will not displace standard techniques. All systems consist of a chamber surrounding the object- and knifeholder ($T \leq -150^{\circ}$ C), which are cooled separately. Usually the object is frozen after pretreatment with cryoprotective and/or encapsulating agents. UTS are prepared from flotation media or from dry knife. Cryofixation (cooling speed) and transfer of UTS to EM seem to be important prerequisits. Although many problems remain, the first results are nevertheless encouraging.

THE PROBLEMS OF ASSESSMENT OF ATP-ASES IN LIGHT AND ELECTRON-MICROSCOPY

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Moses et al /1966/, Rosenthal et al /1969/ have recently found that lead ions are capable of catalyzing the nonenzymatic hydrolysis of nucleoside phosphate. The inorganic phosphate is released by the lead-catalyzed hydrolysis of ATP in the medium. These findings naturally raised questions concerning the validity of the method. The assessment of ATP--ases both in light and electronmicroscopy is not unequivocal. The diffusion of lead phosphate that is produced by the effect of enzyme, the hydrolysis of non-enzymatic substrate and non-specific precipitation of lead may interfer with the reliable assessmen of the enzyme. The above mentioned difficulties jeopardize the value of this method in the follow up and characterization of pathological processes. Liquid scintillation counting method /Lead^{210}/ demonstrated the altered lead binding characteristics of tissues. X-ray microanalysis results suggest that the reaction produced in the fine structural components of the cell is often not in keeping with lead phosphate. The paper includes questions of the non-specific binding of lead in tissue structures /mitochondria, lysosoma, plasma membrane etc./ in connection with the electron--microscopical hystochemical demonstration of nucleoside phosphatases in normal and pathologicel conditions.

EXAMINATION OF POLYSACCHARIDES ON THE CELL SURFACE BY ELECTRON MICROSCOPIC HISTOCHEMICAL METHODS

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The polysaccharides covering the cell surface were studied in preneoplastic and neoplastic alterations of mouse skin, hu - man skin and breast as well as in ascites cells, somatic hybrid cells by means of periodic acid-silver methenamine (PASM) reaction, ruthenium red and Concanavalin A methods. In solid tumours using PASM re - action an increased amount of polysaccharide could be observed on the cell surface. The correlation between the antigenic reactivity and Concanavalin A binding capacity was also investigated. Somatic hybrid line, exhibiting high antigenic reactivity with immunofluorescence and mixed hemadsorption test, showed an increased Concanavalin A and ruthenium red reaction.

The methods mentioned above have different histochemical meaning. PASM reaction has been used for the detection of the quantity of polysaccharides while the Concanavalin A for fructose and furanose constituents only. Ruthenium red technique demonstrates the presence of negatively charged groups on the surface.

PROMT MITOCHONDRIAL CHANGES IN LIVER MITOCHONDRIA OF REHYDRATED RATS

Sz.Virágh, and I.Bartók, and J.Menyhárt, Postgraduate Medical School, Department of Pathological Anatomy, Péterfy Hospital, Department of Pathology and Semmelweis Medical University, Urological Clinic, Budapest, Hungary

Adult laboratory rats were deprived of water for six days. Mitochondrial and ER swelling was the most prominent alteration in the hepatocytes of dehydrated animals. Ten minutes after the start of rehydration with tap water the mitochondrial swelling practically disappeared and a surprising mitochondrial autoreproduction with different symmetrical and irregular forms of division was observed. Man, mitochondria became elongated, at the same time, and longitudinal cristae with the appearance of a periodic intracristal pattern were found. The promt appearance of mitochondrial divisions and inner membrane transformations will be discussed.

APPLICATION OF ENERGY DISPERSIVE X-RAY SPECTROMETRY (EDAX), TRANSMISSION EM AND SCANNING EM TO PATHOLOGY.

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Application Laboratory Electron Optics
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Eindhoven, The Netherlands.

The energy dispersive X-ray analysis of biological specimens studied in the electron microscope can give excellent information on the distribution of elements in the specimen with respect to its morphology. Simultaneous analysis of all elements form Na upwards, using a 1000 channel analyser allows a complete spectrum to be recorded in a few mins. Specially when mounted to a Philips EM 301 electron microscope with goniometer stage the resolution is very good. Elements like K, Na and Ca can be analysed under suitable conditions down to 10^{-16} grams within mins without destruction of the specimen. When X-ray analysis is intended, the preparation technique can be chosen so that no peak overlapping occurs from staining or fixation material and the elements to be identified. E.G. S-peaks can't be identified when OsO_4 fixation and/or Pb staining are applied. Some examples of elemental analysis in pathological/biological specimens will be discussed.

The scanning attachment mounted to the EM 301 on show is a powerful tool in both backscatter and scanning transmission microscopy. The 100kV STEM mode is of high interest for the study of sections in the order of approx. 1 μm thickness. With one instrument it is possible to study the specimens morphology, topography, structure and elemental contents.

EMMA-4 ANALYSIS OF MYOCARDIAL CALCIUM LOCALISATION FOLLOWING DIFFERENT FIXATIONS.

R.Yarom,F.Peters,M.Scripps - Dept.of Path. Hebrew Univ.-Hadassah Med.School Jerusalem Israel and Electron-Microscopy Section of the Cavendish Laboratory, Cambridge - England.

Use of the electron microprobe analysis together with ultrastructural histochemistry and pathological processes, and also may prove useful in assessing the nature and validity of histochemical reactions and techniques. In previous microprobe work we have demonstrated the pyroantimonate precipitation of intracellular calcium. In further studies on calcium localisation, myocardial tissues were fixed in glutaraldehyde, osmium and pyroantimonate in osmium and then examined with the EMMA-4. Unstained gold sections were prepared and many reading of chosen spots were taken in each specimen.

Calcium could be detected with all the fixatives used,but at varying efficiency. Using glutaraldehyde,the amount detected was small and without special localisation except in the nucleus and nucleolus.Osmium fixation showed a much higher, but still poorly localised calcium concentration.Pyroantimonate in osmium produced the highest intracellular calcium concentration,and special binding sites could be demonstrated in the dark parts of the nucleus,mitochondria,tubular junctions and thin filaments.

EMMA 4 IDENTIFICATION AND LOCALIZATION OF GOLD

Yarom R., Stein H., Robin G., Makin M., Hall T.A.

From the Departments of Pathology and Orthopedics, Hebrew University-Hadassah Medical School Jerusalem, Israel and from Cavendish Lab., Cambridge, England.

The recent detection of chromosomal abnormalities after intra-articular radiactive gold administration led us to undertake an extensive study of the mode of action and spread of the gold when injected intra-articularly. It was hoped that the metal would serve as a "built-in" tracer, but it soon became obvious that the electron-dense particles encountered in ultrastructural examinations were not all gold. The electron microscopic microprobe x-ray microanalyser EMMA-4 was used to make positive identifications of the precipitates in human synovial biopsies and in various organs of experimental animals.

ELECTRON MICROSCOPY IN ROUTINE PATHOLOGY

Round table

Organized by

DUSTIN, P.

Invited participants

BIAGINI, G., BRAGAGLIA, M. M., SCALA, C., BORSETTI, G., LASCHI, R.

DUSTIN, P.
FARDEAU, M.
GIESEKING, R.
GRONIOWSZKI, J.
HASSOUN, J., GAMBARELLI, D., TRIPIER, M. F., BERARD, M., TOGA, M.
HULTQUIST, G., GRIMELIUS, L., WESTERMARK, P.
HÜBNER, G.
KÁDÁR, A., MOLNÁR, E., BUCSKY, P., LÁNCZOS, F., JELLINEK, H.
LAPIS, K.
LASCHI, R., BIAGINI, G. SIMONI, P.
ORMOS, J., MONUS, Z., CSAPO, ZS.
RADNOT, M.

ELECTRON MIOROSCOPIC STUDIES IN CHRONIC FAMILIAL JAUNDICE

Almási,Susana; Feszt,Tibor; Filep, Victor and Kasza, Ladislau
Institute of Medicine and Pharmacy,Dept.of Histology; Research Centre of the Academy of Medical Sciences, Tirgu-Mures,Romania

The authors used electron microscopy in the study of liver needle biopsies from 17 cases of Gilbert's disease,Dublin-Johnson or Rotor syndromes.They always found cell membrane alterations.In Gilbert's disease the number of microvilli is reduced,the electron density of the thickened plasmolemma became discontinuous and collagen fibres appeared in the intercellular and Disse spaces. In the D-J. and Rotor syndr.,the cellular membrane became flattened,discontinuity of the electron density occured.The intercellulare spaces are dilated.Dilatation,degranulation,fragmentation of the endoplasmic reticulum and increase of free ribosomes was observed in evry case.The alteration of mitochondria could be observed in all cases,accompanied by the appearing of filamentary and vesicular inclusions appear in the same liver cells or mitochondria. The deposit of lipofuscin granules and biliary pigments was observed in all cases. In D-J.syndr. the specific polymorph pigment is present.In Rotor syndr.numerous vacuoles containing lipoproteic-pigment were observed.The observed ultrastructural signs of repair explain the non-evolutive character of these syndromes.

ELECTRONMICROSCOPICAL STUDY OF INFANT'S LIVER BIOPSIES

Martha Balazs, V.F.Lukács, and J.Dénes
Postgraduate Medical School, Department of Pathological Anatomy and Apathy Pediatric Hospital, 2nd Department of Internal Medicine and 1st Department of Surgery, Budapest, Hungary

In cases of congenital bile duct atresia electronmicroscopical signs of cholestasis and obstruction of sinusoids caused by enlarged Kupffer-cells were found. It has been supposed that the disturbances of microcirculation are also a causing factor concerning the liver cell lesion.
In cases of "inspissated-bile-syndroma" the cholestasis and damages of liver cell organelles were less pronounced than in cases of bile duct atresia. Also the clinical autcome was benign. The cholangiodysplastic pseudocirrhosis is rare. In these cases the marked signs of migration of leukocytes mean a decreased cohesion of the epithelial cells. When dedifferentiated liver cell carcinoma was found, their electronmicroscopical examination helped the punctual classification of the tumour.

ELECTRONMICROSCOPY OF CRYSTALLOID INCLUSION IN HEPATOCYTES AND KERATINOCYTES

Bednář Blahoslav
Hlava Institute of Pathology,Charles Univ Prague, Czechoslovakia

Crystalloid inclusions were studied in 500 liver biopsies and 400 skin biopsies by electronmicroscopy.

Most frequently linear crystalloid inclusions occured in mitochondria, particularly in the damaged hepatocytes. Their origin and significance is not clear.

Some crystalloid virions occuring intranuclearly, were occasionally found also in the cytoplasm of keratinocytes and histiocytes due to destruction of nuclei and fagocytosis of virions.

Hexagonal crystals of paraprotein were found in the cytoplasm of some hepatocytes of one patient suffering from IgA myeloma. Identical crystals were present in the cisternae of rough endoplasmic reticulum of bone marrow plasmocytes of this patient.

Intranuclear filamentous finely crossed and asteroid inclusions were detected in hepatocytes and keratinocytes in six cases. Their origin from capsids is suggested as they were revealed several times simultaneously with virions of papovavirus.

TECHNICAL IMPROVEMENTS FOR ULTRASTRUCTURAL INVESTIGATION IN DIAGNOSTIC PATHOLOGY

Biagini,Graziella, Bregeglia,M.Mercedes,Scala, Cesare, Borsetti,Giampaolo and Leschi,Renzo.
Istituto di Microscopia elettronica clinica, Bologna, Italy.

A rapid embedding procedure for preparing bioptic and autoptic materials both for light and electron microscope investigation is described.
This procedure requires the use of powder anhydrides as hardeners for epoxy resin (Araldite). The obtained embedding medium allows to produce, with a short polimerization at low temperature, soft bloks for cutting very large semithin sections.The same bloks, with a further brief polymerization at high temperature, can be used for obtaining thin sections very stable under the electron beam also without carbon coating.
Some simple methods for specific staining of tissue components on semi-thin sections have been developed.
The usefulness of these techniques in routine diagnostic pathology is discussed.

DATA ON THE ULTRASTRUCTURE OF ODONTOGEN CYSTS

Csiba, Á. and Korányi-Both, A.

Maxillo-facial Surgery and Dentistry and 1st Institute of Pathology, Semmelweis Medical University, Budapest, Hungary.

Authors examined 10 odontogen cysts light and electron microscopically.

Their results show that there exists the possibility to differentiate between keratinized and non-keratinized cysts. The cells of both types were rich in cell organelles, glycogen and tonofibrils. The nuclei of the cells were generally oval and mildly lobulated. The intercellular spaces contained numerous fragments of cell organelles. In the connective tissue relatively few structures were observable. Under the intact basement membrane aperiodical fibrils were also observed besides the collagen fibers. With regard to their ultrastructure these fibrils are suggested to be oxytalan fibers.

ELECTRON MICROSCOPY IN ROUTINE PATHOLOGY

Dustin, Pierre

Department of Pathology, University of Brussels, Belgium

In our Department, electron microscopy is used more and more often for various problems, and has provided important information in the following fields : storage diseases (identification of the ultrastructure of lipid and mucopolysaccharide intralysosomal inclusions); amyloidosis; paraneoplastic endocrine secretions (demonstration of secretory granules in small cell carcinomas of the lung); myxoedema (abnormal thyroid cells; thyrotropic cells in the pituitary); thymus pathology (formation of lamellar lipid inclusions in thymic atrophy); identification of difficult tumors (gastric glomangioma). Some information has recently been gathered by scanning electron microscopy in thyroid adenomas. Electron microscopy - both transmission and scanning - has become an indispensable tool in the Pathology Department of any University hospital.

RUTINE APPLICATION OF ELECTRON MICROSCOPY IN CLINICAL DIAGNOSTICS.

Judith Derócsy,
Clinic for Dermatology, Semmelweis Medical University, Budapest-Hungary.

1./ Dermatomyositis: paramyxovirus particles were found in the cytoplasm of musole and vessel-endothel cells. In certain cases of dermatomyositis /following a febrile upper respirstory disease/ the demonstration of virus is of diagnostic significance. The number of inclusions is in direct relation with the "activity" of the disease.

2./ The malignant reticulosis type of histiocytosis X. In the histiocytes are demonstrable certain commashaped bodies which actually are convoluted tubules of internal periodicity and of 300 Å diameter. They develop either as result of pathological differentiation of ergastoplasmic tubules or invaginations of the cytoplasmic membrane.

3./ Hairy cells in myeloma. The hairy cells were found not to be specific for leukemic reticuloendotheliosis but to develop as a variation of the ergastoplasm of proliferating lymphatic plasma cells.

ULTRASTRUCTURE OF GRANULOMATOUS RHINOSCLEROMA.

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Postgraduate Medical School, Department of Pathological Anatomy and Department of Otorhinolaringology, Budapest, Hungary

Granulomatous lesion of rhinoscleroma of a 48 year old man had been studied electronmicroscopically. All of the characteristics of this lesion were present in the tissue examined. There was a marked vacuolisation of the cytoplasm of Mikulicz cells, and relatively few organelles were present. The content of the vacuoles consisted of a granular, loose material and some compact substance, which showed higher electrondensity. The Klebsiella rhinoscleromatis could be also observed within these vacuoles. Ther was a pronounced, clear cuffing around the microbes, which probably represented their capsule.

The origin of the Mikulicz cells is still obscure. According to different authors they are originated from histiocytes, but the possibility of the plasma cell origin has been also discussed.

CONTRIBUTION OF THE ELECTRON MICROSCOPY IN ROUTINE MUSCLE PATHOLOGY.

M.Fardeau, Service de Microscopie Electronique Division Risler, Hopital de la Salpetriere, Paris-France

Electron microscopy has allowed important progresses in muscular pathology, particularly in the analysis of elementary lesions and in the identification of new entities within the group of congenital myopathies. However, the interpretation of electron microscopic data has met two main obstacles: 1/ the non-specificity of most of the ultrastructural changes; 2/ the difficulty of a quantitative study of these changes. Thus, the diagnostic utilization of electron microscopy in muscle pathology must be regarded only a complementary investigation besides histo-enzymologic technics and motor innervation studies.

ULTRASTRUCTURAL DIFFERENTIAL CHARACTERISTICS OF OBSTRUCTIVE AND HEPATOCELLULAR CHOLESTASIS

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Porto - Portugal

Ultrastructural study of hepatic biopsies performed during the initial phases of cholestasis in rats,revealed distinctive morphological features between extrahepatic cholestasis,obtained by common bile duct ligation,and intrahepatic cholestasis,obtained by choleperitoneum and alpha naphtylisothiocynate (ANIT) intoxication. These characteristics concern the structures and organelles of the hepatocyte,namely mitochondria, lysossomes,endoplasmic reticulum,GOLGI apparatus and bile canaliculi.

These findings are considered valuable elements in the differential diagnosis between obstructive and hepatocellular cholestasis.

APPLICATION DE LA METHODE RAPIDE EN MICROSCOPIE ELECTRONIQUE POUR LA DETECTION DES PARTICULES DE TYPE VIRAL AU COURS DES HEPATITES AVEC ANTIGENE AUSTRALIA.

Feroldi,J., Leung Tack Ki,A., Labor.d'Anat. Path. Univ.Claude Bernard, Lyon-France.

SOME EXAMPLES FOR THE APPLICATION OF ELECTRON MICROSCOPY ON BIOPSY SPECIMENS

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VISUALIZATION OF ALVEOLAR LINING LAYER OF THE LUNGS IN SMALL /BIOPSY/ SAMPLES

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Department of Pathological Anatomy
Medical Academy, Warsaw, Poland

It is difficult to use electron microscopy for evaluation of alveolar lining layer in small samples of biopsy material. A simple preparatory procedure for electron microscopy could corroborate in some way with routine light microscopy biopsy applied largely in lung pathology today. According to this line a procedure based on vapour fixation has been elaborated in rat lungs /J.Groniowski and M.Walski, in press/. Biopsy samples from subpleural parts of the lung taken from intraperitoneally anesthetized rats were exposed to osmium tetroxide vapours in a glass-syringe. During the vapour fixation the "respiratory movements" of the piston were performed every 15 sec. for a period not shorter than 120 sec. Postfixation, in 3.6% glutaraldehyde phosphate buffered at pH 7.4 for 1 hr at 0°C and in 2 % osmium tetroxide for 1 hr at 0°C, followed. The total period of dehydration with acetone was 12 min. The samples were embedded in Epon 812. Uncontrasted and lead citrate stained sections were studied.

Vapour fixation, prior to fixation by immersion, combined with a rapid dehydration results in good preservation of alveolar lining layer in the biopsy material. Repeated changes of the gas pressure seem to improve the obtained results, significantly.

CONCENTRIC LAMINATED BODIES IN MUSCLE PATHOLOGY.

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Described at the first time by Luft and al. /1962/ the concentric laminated bodies/CLB/ were found of various number in sarcoplasm under plasmalemma. These profiles ranging from 0,4 to 5 microns were ovoid or concentrical in shape. In their center glycogen granules, mitochondrias or vesicles occurred. Their wall structure consisted of 3 to 15 lamellae, 60 Å thick with a periodicity of 100 Å. Regularly disposed osmiophilic densities were noticed close to lamellae, giving them a periodic transversal striation. CLB limits were not clearly defined without any bound unit-membrane. In previous papers mitochondrial origin of CLB was put forward; in the present study, the myofilamentous origin seemed obvious, according to relations between CLB and sarcomeric actine filaments. Moreover CLB and filamentous bundles observed in normal and pathological muscle fibres showed similar patterns; transitional forms between these two types of filamentous inclusions were noticed by the authors. CLB pathogenesis had been doubtful till now. These profiles might be interpreted either as a re-arrangement or as a re-formation of myofilaments in pathological muscle fibres.

ELECTRON MICROSCOPIC EXAMINATION OF BIOPSY AND AUTOPSY SPECIMENS AS AN AID IN CLINICAL PATHOLOGY

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Electron microscopic(EM) examination may be a valuable complement to light microscopic(LM)diagnosis in clinical pathology. Above all it can give additional information concerning structures which cannot be observed at all or not distinctly enough by light microscopy, e.g. details of secretion granules of endocrine cells, fibrils, virus and inclusion bodies; details of importance for determination of the type of tumour cells.
EM examination cannot replace LM examination as a routine technique, as

it does not allow application of histochemical staining methods and a general survey of the specimen to an equal extent to LM;

the current embedding technique is more circumstantial and time-consuming

We have tried the following embedding techniques for EM examination of biopsy and autopsy material:

1. unfixed specimens were divided and put in different fixatives for LM and EM;

2. fixed specimens (usually formalin) were post-fixed for EM (glutaraldehyde, OsO_4);

3. sections from paraffin blocks were post-fixed as above and embedded for EM. Areas with focal changes can be chosen from the paraffin sections. The paraffin sections can be pretreated e.g. for analysis of heavy metals;

4. from stained slides the sections were detached, post-fixed and embedded as above.

Slides from selected cases will be showed.

POSSIBILITIES AND LIMITS OF FINE STRUCTURAL ANALYSIS OF FORMALIN-FIXED AND PARAFFIN EMBEDDED HUMAN BIOPSY AND AUTOPSY SPECIMEN.

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The fine structural analysis of paraffine-embedded biopsy and autopsy specimen of human tissues has proved to be a very useful diagnostic tool. Since the preservation of tissue depends mainly on the quality of the initial fixation, biopsy specimen give better results than autopsy material. Nevertheless many fine structural details of normal and diseased cells, as nuclear components, ergastoplasm, cell inclusions (glycogen, fat droplets, pigments and other dense bodies), basement membranes and fibrillar interstitial material as collagen, amyloid or fibrin, can be identified by the fine structure also in autopsy specimen. The fine structural investigation is especially useful in the differential diagnosis of pigment bodies in liver cells (Dubin-Johnson pigment, drug pigment, lipopigments), in storage diseases (glycogenosis), in the diagnosis of glomerular lesions (glomerulonephritis, eclampsia), and in the determination of tumor cell differentiation (f.i. specific granules in carcinoid tumor cells). It also is adventageaous in the detection and identification of protocoa and viruses, particularly of the herpes-cytomegaly group. - It is our opinion that electron microscopic investigation also in routine pathology is possible and can help to optimize the histologic diagnostic procedures

RAPID TECHNIQUES FOR ELECTRON MICROSCOPY OF RENAL BIOPSIES

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A rapid preparation technique is presented which makes it possible to study ultrathin sections in the electron microscope within 5 hours after the biopsy has been taken.

Preparation procedure in brief:
0.5 mm tissue pieces.
Fixation:
4 % glutaraldehyde and 2 % osmium tetroxide for 30 min. each at room temperature.
Dehydration:
Graded alcohols (30 min).
Embedding:
Epon (propylene oxide as an intermedium) A:B = 4:6.
Polymerization:
70°C for 45 min. and 105°C for 75 min.
Results:
The ultrathin sections (obtained with glass-knives) are of the same quality as those obtained after the standard slow preparation procedure.

References:

Johannessen,J.V.: Rapid Ultrastructural Diagnosis in Human Kidney Disease, J. Ultrastruct. Res., in press.
Johannessen,J.V.: Rapid Processing of Kidney Biopsies for Electron Microscopy, Kidney International,vol. 3 (1973), pp. 46-50.

ELECTRON MICROSCOPIC STUDIES ON KIDNEY BIOPSY SPECIMENS FROM CHILDREN.

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A total of 17 biopsy specimens of different origin was studied. The clinical diagnosis was nephrosis syndrome and hematuria /nephritis?/ in 14 and 3 cases,respectively. The patients had histories of 6 months to 9 years at the time of the biopsies.

The morphological diagnoses obtained by examining normal and ultrathin sections were evaluated as to their possible clinical use. Electron microscopy may be of importance in obtaining correct histological diagnosis. This,however,appears to be of moderate clinical importance since as yet there are no specific drugs available to permit selective treatment of the different glomerular lesions representing the morphological substrate of the clinically uniform "nephrosis syndrome".

In cases of asymptomatic hematuria with the possibility of nephritis electron microscopy may be of considerable use in judgeing prognosis and decideing therapy.

ULTRASTRUCTURAL CHANGES OF HEPATOCYTES IN PATIENTS EXPOSED TO VARIOUS CHEMICALS.

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This study was undertaken to present light-, and electron microscopic changes of liver cells of individuals exposed to the effect of some organic compounds and showing clinical and laboratory signs of acute or chronic liver injury.

In two cases of acute accidental carbon-tetrachloride and in one case of petrol poisoning /all of them men/, apart from fatty changes and various types of cellular necrosis, mitochondrial changes /enormously increased electron density of the matrix in the l.case of CCl_4 poisoning; osmiophilic droplets of various shape and size in the other one; spherical electron dense bodies with electron opaque centre in petrol poisoning/ were most striking.In a woman,dealing with TNT, bizarre-shaped and giant mitochondria with cristalline inclusions in their highly dense matrix and focal cytoplasmic areas of fibrillar structures were present.In two men working with organic solvents lipid droplets, mitochondrial changes /swelling,increased electrondensity of the matrix/ and alterations of the rER /from mild to severe dilatation of the cysternae/ were encountered.

FINE STRUCTURAL STUDIES IN MYASTHENIA GRAVIS

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1st Institute of Pathology, Semmelweis Medical University and Department of Neurology, Róbert Károly Hospital, Budapest, Hungary.

The muscle biopsy samples of 23 patients suffering from myasthenia gravis were studied electron microscopically. The fine structural changes of the neuromuscular junctions were examined.

It is suggested on the basis of electron microscopic observations that the alterations of the synaptic gap may delay or inhibit the diffusion of acetylcholin to the postsynaptic receptors. In an advanced stage of the disease the fine structural changes produced a denervation in the neuromuscular space.

A certain relationship is suggested to exist between the autoimmune mechanisms involved in certain cases of myasthenia gravis and the fine structural alterations registered.

ELECTRON MICROSCOPY IN LIVER PATHOLOGY

Krustev, Luka and Poljakova-Krusteva, Olga
Center of Hygiene, Dept. of Pathology, Sofia, Bulgaria

100 biopsies have been studied electronmicroscopically. Cases of cirrhosis, hepatitis, cholestasis, cancer of the liver, hyperbilirubinemias, fatty liver and some others are concerned.

Results are discussed in the light of the various diseases. At the same time, the ultrastructural changes are grouped in "syndroms" having a more general meaning. Such are activation of lysosomes in inflammatory processes of the liver, adaptation changes in endoplasmic reticulum after nutritional or toxic factors etc.

The data is also discussed in correlation with experiments on different animals. Although electron microscopy can have a diagnostic meaning it is still more to be applied in understanding the substance of the pathological process as well as to bridge the gap between liver structure and function.

THE USE OF THE FINE STRUCTURAL ANALYSIS OF LIVER BIOPSY SPECIMENS

Lapis, Károly
Ist Institute of Pathology, Semmelweis Medical University, Budapest, Hungary.

Liver needle biopsy specimens of 716 patients with various liver diseases were studied by electron microscopy. In 14 cases with constitutional hepatic dysfunction /Dubin-Johnson, Gilbert and Rotor syndrome/ it was possible a further differentiation of the pigments accumulated in the hepatocytes and there were crystalloid inclusions consisting mostly of pronase and pepsin digestible protein found in the mitochondria. The rEr was decreased whereas the sEr was increased. In 50 cases of intra- and extrahepatic cholestasis the study of the alterations of bile canaliculi and bile deposits could help to clarify the pathogenesis of icterus. After toxic liver injury /alcoholic liver, drug hepatitis/ increase of sEr was noticed. In 120 cases of acut viral hepatitis and chronic /aggressive and persistent/ hepatitis no infectious agent was observable but the ultrastructural analysis was useful to establish the degree of liver parenchyma injury. The study of the structure of human hepatomas revealed pleomorphism of the cell nuclei, great numbers of cytoplasmic foldings into the nuclei, enlargement of the nucleoli, fingerprint-like formations of Er and a decrease of glycogen granules.

ELECTRON MICROSCOPE INVESTIGATION ON BLOOD CELLS IN THE COURSE OF DIFFERENT STORAGE DISEASES.

Lacchi,B., Biagini Graziella, Simoni,P.,
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The peripheral blood of young patients suffering from metabolic disorders /mucopolysaccharidoses, lipidoses/ has been studied by electron microscopy to see whether it was possible identifying specific storage bodies into the blood cell cytoplasm.

The analysis has been extended to the relatives of the patients.

POSSIBLE VIRAL ETIOLOGY IN RHEUMATOID ARTHRITIS

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In previous reports characteristic nuclear bodies and virus-like particles were demonstrated in rheumatoid synovial membrane /Ann.rheum.Dis.1971.,Scand.J.Rheum.1973/. According to the performed ultrastructural investigations the conclusion could be drawn with strong probability on the presence of some kind of paramyxovirus or its multiplication forms. Therefore, measles antibodies were measured in the sera of patients with rheumatoid arthritis. 22% of the tested patients had higher haemagglutination inhibition antibody titers to measles virus in comparison to the normal population from the same age groups. Nevertheless, the ultrastructural investigations cannot be excluded that some other virus or viruses may have a role in the development of the alterations observed in rheumatoid synovial membrane. According to our observations it is likely that same form of viral infection may have a role in the pathogenesis of rheumatoid arthritis.

ELECTRON MICROSCOPY OF LIVER BIOPSIES IN ICTERIC STATES

Ormos, Jenő; Mónus, Zoltán and Csapó, Zsolt

Department of Pathology, Medical University, Szeged, Hungary

In primary biliary cirrhosis /non-suppurative destructive cholangitis/ as well as in biliary atresia the bile secretory apparatus /hepatocytes and their bile canaliculi/ ultrastructurally appear to be normal in early phases. The regurgitation of the bile secreted by the hepatocytes is due to the resorption by the damaged ductular cells. Further studies performed in these conditions give additional data to the fine structure of hepatocellular and ductular damage as well as mesenchymal reaction and fibrogenesis resulting in cirrhosis. Obstructive jaundice, chronic hepatitis and various forms of hyperbilirubinaemia can be differentiated ultrastructurally from the above mentioned states, but clinical data must also be taken into consideration.

MITOCHONDRIAL CHANGES IN THE ORBICULARIS OCULI MUSCLE.

Radnót, Magda

First Eye Clinic, Budapest, Hungary

Muscle specimens of the orbicularis oculi were studied electron microscopically. The patients were operated for senile entropion and ectropion, respectively. Grave destruction of the muscular elements as well as vacuoles among the muscle fibres could be observed. The number of mitochondria considerably increased in the subsarcolemmal area. In the mitochondria, which were of different sizes, in some places greatly enlarged and bizzarely shaped, there were inclusions of crystalline structure. Also among the muscle fibres the number of mitochondria increased, in many places they were huge and in some the above-mentioned inclusion bodies could be seen. Besides, in some areas the so-called "fingerprint bodies" could equally be found with or without crystalline inclusions - in some places considerably numerous. These changes have been so far found in the case of various myopathies. Present findings speak for the possibility that similar changes may occur in the case of senile muscle atrophy.

ELECTRONMICROSCOPIC EXAMINATION OF LYMPH VESSELS IN PATIENTS WITH RECURRENT ERYSIPELAS

Schneider, Imre, Thury, Géza and Párducz Árpád

Dept. of Dermatology, Roentgenology, Univ. Med. School, Szeged and Biological Research Center Hungarian Academy of Sciences, Szeged, Hungary

Inflammatory changes of lymph vessels manifesting in erysipelas recidivans are well -known. As only a few data are available regarding the histopathology of lymph vessels, electronmicroscopic examination of prefascial lymph vessels from the dorsal part of the legs was carried out prior to lymphangiography in the case of 33 patients suffering from recurrent erysipelas localised on the lower extremities. Lymphedema could be observed on the site of inflammation in most of the cases. Normal lymph vessels could be demonstrated both on the normal and pathologic sites. Partial separation and dilatation of interendothelial junctions were seen in lymphangiectasia and different conditions of lymphangitis /endolymphangitis proliferans, lymphangitis simplex chronica/. "Striated filamentous bundles" could be demonstrated near the cytocentre of the endothelial cell in a patient with lymphangiectasia. System of "fine filaments" could be observed in the endothelial cells of both pathological and normal lymph vessels. In lymphangiectasia pinocytotic vesicles could be primarily demonstrated in the basal part of endothelial cells.

LIGHT AND ELECTRON MICROSCOPIC CYTOCHEMISTRY OF LEUKAEMIC LEUCOCYTES

K. Szilágyi, I. Orbán, Ilona Gálfi and G. Kelényi

Dept. of Pathology and Pediatric Clinic, Med. Univ., Pécs and Dept. of Pathology, County Hospital, Kaposvár

Light and electron microscopic cytochemistry of leukaemic cells proved to be a valuable method for differentiating certain types of haemoblastoses. Knowledge of the origin of the leukaemic cells is important for adequate therapeutic measures.

In the blood cells with Auer bodies and pseudo-Pelger nuclear anomaly of an acute promyelocytic leukaemia the azurophil granules showed anisotropic staining with azur A, intense peroxidase, naphtylacetate-esterase and acid phosphatase reaction. The submicroscopic structure of the granules and especially that of the Auer bodies were similar to the azurophil granules of lower vertebrates.

In a 2 and 1/2-year-old patient with acute leukaemia the origin of the leukaemic cells could not be established with the usual staining methods. The peroxidase and sudan black B negative cells showed a fine granulation with the PAS-reaction, their naphtol-DS-chloroacetate-esterase reaction appeared weakly, the naphtylacetate-esterase intensely positive. In the electron microscope the leukaemic cells contained electron dense granules. On the basis of these findings the case was regarded as acute monocytic leukaemia.

AN ATTEMPT OF DIFFERENTIAL DIAGNOSIS OF ACUTE LEUKEMIAS IN CHILDREN BY MEANS OF ELECTRON MICROSCOPY

Topiłko Andrzej and Radwańska Urszula

Institute of Biostructure and Institute of Pediatrics, Medical Academy, Poznań

The electron-microscopic examinations of bone marrow were performed in 13 children with acute leukemia. Thanks to these examinations we recognized 4 cases of non-differentiated leukemia as lymphoblastic ones. Our results indicated also, that electron microscopy is useful in diagnosis of myeloblastic leukemias. It allowed to show in some blast- cell the presence of very young azurophilic granules in channels of Golgi complex.

The authors recommend the electron-microscopy in cases when the aplication of the rutine cytochemical examinations fail.

ULTRASTRUCTURAL EXAMINATION OF THE EXPERIMENTALLY INDUCED AND HUMAN MAMMARY TUMOURS

Tóth, József and Csuka, Orsolya
Research Institute of Oncopathology
Budapest, Hungary

We have studied the fine structure of the mammary tumours induced in Wistar female rats by 7,12-dimethylbenz/a/ anthracene /Huggins tumour/, as well as the human breast fibroadenomas, papillomas and carcinomas by electron microscopical and electron histochemical methods i.e. by Mg^{++} dependent ATPase and UTPase, periodic acid-silver methenamine /PASM/ reaction.

Histochemical characteristics and fine structure of induced tumours have a similarity to benign human breast tumours.

The proliferation of myoepithelium is the most prominent in the benign human breast tumours. The myoepithelial origin was demonstrable in none of the histological types of human breast cancer.

The most consistent fine structural property of the degree of the clinical malignancy is the lack, or diminishing of the cell junctioning apparates, lack of the electron microscopical basement membrane and the decrease of the cytoplasmic organelles in number.

ULTRASTRUCTURAL CHANGES IN HUMAN MYOCARDIUM DURING OPEN HEART SURGERY.

Varga,T., Somogyi,E., Soós,J., Békássy,Sz., Arvay,A.

Institute of Forensic Medicine, Semmelweis Medical University, and National Heart Institute, Budapest, Hungary

Human myocardial lesions caused by anoxaemia have been investigated. The material was taken from the atrial and ventricular musculature before and after cross-clamping of the aorta of 20 patients having been operated in extracorporeal circulation.

After 10 minutes of anoxaemia we have not seen any lesion in the myocardium. After 15-20 minutes of anoxaemia decrease of the glycogen content, intracellulare oedema, dilatation of the sarcoplasmatic reticulum and swelling of the mitochondria have been revealed. After more than 30 minutes of cross-clamping intramitochondrial dense particula, margination of the nuclear chromatin have appeared. Lesions of the capillary endothel have not been noticed. The morphological changes revealed have been similar in the atrial and ventricular myocardium.

EXPERIENCES ON ELECTRONMICROSCOPICAL EXAMINATION OF 140 HUMAN LIVER BIOPSIES.

S.Várkonyi, Márta Balázs

Postgraduate Medical School, Department of Pathological Anatomy and MAV Hospital, 3rd Department of Internal Medicine, Budapest, Hungary

The ultrastructure of chronic persistent hepatitis and chronic agressivehepatitis was compared. In cases of chronic agressive hepatitis the proliferation and the increased activity of the connective tissue cells was considered to be the primary lesion, and the changes of parenchymal cells as consecutive damages. In early stages of virus hepatitis an important swelling of the endoplasmic reticulum and mitochondrial alterations were observed. In cases of porphyria cutanea tarda damages of mitochondria and accumulation of haemosiderin were the constant findings. As far as the alcoholic hepatic alteration is concerned, the increasing of the connective tissue earlier could be detected by electronmicroscope than by light microscope. In cases of portal cirrhosis the collagen fibres appeared not only in the wall of sinusoids, but also in the intercellular spaces. A few cases of enlargement of liver with unknown origin had also been studied. In these patients anamnesis a chronic abusus of hypnotics was evident. The electronmicroscopical changes consisted of an increasing in number of the tubules of smooth-surfaced endoplasmic reticulum.

ROUTINE ELECTRON MICROSCOPY IN PATHOLOGY

Wijngaarden, J.D. van
Application Laboratory Electron Optics
N.V. Philips' Gloeilampenfabrieken
Eindhoven, The Netherlands.

Electron microscopy need no longer be relegated to the realm of research but is today rapidly becoming a useful diagnostic tool of the pathologist. Although its use on every specimen is impractical and in fact wasteful at our present level of knowledge, the electron microscopic examination of surgical specimens and selected autopsy specimens is every bit as practical and useful as many of the "special" stains routinely employed in many pathology laboratories. Two factors are of deciding importance when discussing the introduction of electron microscopy in diagnostic pathology. The first factor is the availability of a reproducible routine preparation technique which enables a diagnosis to be made within a working day. A short description and some results of such a technique will be presented. The second factor is the presence of a routine electron microscope able to produce good micrographs, even in the hands of a relatively inexperienced laboratory assistent. The Philips EM 201, on show here, is a very suitable instrument for this purpose.

THE SCANNING ELECTRON MICROSCOPY

Organized by

GARDNER, D. L.

Invited lecturers

ALONSO, J.
AMICI, F.
ARAKAWA, M.
BALASSE, P.
CASANOVA, S., BRAGAGLIA, M. M., CORRADO, F.
LASCHI, R.
ENGSTRÖM, B.
GARDNER, D. L.
GRONIOWSZKI, J., WALSKI
KETELBANT
KUHN, Ch.
MILLINGTON, P. F., GIBSON, T., EVANS, J.
WILKINSON, R.
MILLINGTON, P. F., MULHOLLAND, R.
ORFANOS, C. E., MAHRLE, G.
TOKUNAGA, J.
TOSTI, A., VILLARDITA, S., FAZZINI, M. L.

KIDNEY STONES WITH SCANNING ELECTRON MICROSCOPY.

Alonso,I., Univ.Politechnica de Valencia, Valencia-Spain.

SCANNING ELECTRON MICROSCOPY OF ARTICULAR SURFACES OF RABBIT KNEE JOINT. FEATURES IN NORMAL CONDITIONS AND AFTER EXPERIMENTAL IMMOBILIZATION.

Federico Amici, Orthopaedic and Traumatological Hospital. University of Rome. Italy.

Material. These two investigations have been done on male and female adult rabbits. The immobilization has been carried out on 40 animals: the left knees were immobilized by a plaster cast from two up to sixteen weeks. The right knees served as controls.

Method. The specimens (1x1x1,5 cm) were rinsed in isotonic saline solution, then fixed in 2,5% glutaralde hyde buffered in phosphate at pH 7,4. afterwards these specimens have been passed through freeze- drying equipment, glued to a specimen stub, coated with gold or gold-palladium in a Jee-4B vacuum evaporator and examined in a JSM-U3 Scanning Electron Microscope.

Results. The surfaces in normal conditions have shown many different features represented by diffuse roughness, mountlike elevations alternating with depressions ridges with parallel and regular orientation, lacunae of variable size and form, shallow hollows and prominences etc. After immobilization: The joints surfaces have shown changes, the severity of wich was directly connected to the lenght of immobilization's period. These features are represented by irregularity of the surface, eroslons of variable size and form till the appearing of the collagen fibrils due to the deterioration of the ground substance.

SCANNING ELECTRON MICROSCOPE STUDIES OF THE GLOMERULUS IN NORMAL AND SOME PATHOLOGIC SITUATIONS

Masaaki Arakawa, M.D.
Department of Medicine, Kawasaki Medical College, Okayama City, Japan

The glomerulus of normal rats, rabbits, and man was studied by scanning electron microscopy. The podocyte extended several primary cytoplasmic processes which wound transversely around the capillary loops. Some of them projected thin secondary processes, which occasionally gave rise to tertiary processes. From these processes many clubbed thinner terminal processes emerged at a right angle like fern leaves and anchored on the basement membrane. They were interdigitated with each other 3-dimensionally. The neighboring processes came always from different cells.

In aminonucleoside-nephrotic rats, there remained no interdigitation of terminal processes and cells faced adjacent cells over straight cell borders. That indicate that the fusion of the terminal processes is not due to syncytial formation but rather to swelling and retraction of the processes. The same findings were obtained in the glomerulus of a nephrotic patient.

In Masugi-nephritic rabbits, the capillary loops were collapsed and the podocyte increased in number. The cytoplasmic processes were markedly atrophied with mild degree of loss of terminal processes. Some glomeruli were covered with rather homogeneous, partly granular jelly-like substance or irregularly-shaped board-like substance piled up like roof tiles, which might be corresponded to proteinous exsudate in Bowman's space and fibrous crescent respectively seen in light microscopy.

THE USE OF SILVER AS AN ELECTRON STAIN FOR ENDOTHELIAL CELL BORDERS IN THE S.E.M.

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Impregnation of exposed endothelial surfaces by a silver nitrate solution, followed by cobaltous and ammonium bromide conversion and subsequent aldehyde reduction to metallic silver is a method known from the ancient light microscopic histotechnique, which recently was adapted for use in the scanning electron microscope (S.E.M.). It will be demonstrated that by this method, endothelial cell borders can be visualized in the S.E.M., but that the silver grains, which marks the cell borders are not located between the endothelial cells, but on top of the cell surface near the cleft between the two endothelial cells. Arguments will be presented that the silver grains deposited in the inter-endothelial and sub-endothelial spaces, which contribute to the cell delineation in the light microscopic surface preparations, do not contribute to the image formation in the S.E.M.. Moreover it will be shown, that the silver lines obtained by the impregnation of aldehyde-fixed vascular tissue by silver nitrate and cobaltous and ammonium bromide do contribute to the appearance of silver lines in the light microscopic preparations but not to the silver deposits in the cell border region in the S.E.M.. It will be shown that vascular perfusion of a 2% silver proteinate solution at neutral pH and subsequent reduction by aldehyde perfusion fixation results in a similar delineation of the cell borders by silver grains, as with silver nitrate.

SCANNING ELECTRON MICROSCOPE OBSERVATIONS ON HUMAN BLADDER IN NORMAL AND PATHOLOGICAL CONDITIONS.

Casanova, Silvia, Bragaglia, Mercedes, Simoni, Paolo, Corrado, Franco and Leschi, Renzo

Istituto di Microscopia elettronica clinica and Ospedale Malpighi, Bologna, Italy.

The fine structure of the human bladder in pathological conditions has been till now studied expecially by means of transmission electron microscopy, while very scarce are scanning electron microscope studies on this organ, both in normal and in pathological conditions (Fulker, Cooper and Tanaka, 1971; Skoluda, Wegner and Richter, 1972).
The present investigation is mainly concerned with the setting of a good preperation technique for maintaining the relationships between the cells of the bladder epithelium in byoptic specimens obtained by transurethral endoscopic resection or by surgical excision.
Preliminary observations have been carried out on ultrastructural modifications in some pathological conditions.

Fulker, Cooper and Tanaka, Cancer, 27, 71 (1971)

Skoluda, Wegner and Richter, Der Urologe, 11, 338 (1972).

SCANNING ELECTRON MICROSCOPY IN THE STUDY OF THE NORMAL AND PATHOLOGICALLY ALTERED INNER EAR.

Engström, Berit, Res.engineer, Dept.of oto-rhino-laryngology, Akademiska sjukhuset, Uppsala - Sweden.

Scanning electron microscopy, SEM, has been used for a study of normal and pathologic inner ears of animals and man. A simultaneous study of comparable materials has been made using transmission electron microscopy, TEM. The inner ear sensory regions contain cells provided with very characteristic surfaceorganelles, stereocilia, kinocilia and microvilli. The sensory cells have rich neural contacts and the organ of Corti contains neural pathways and nerve endings which can be visualized in a beautiful three-dimensional manner. Small or extensive regions of damage after noise exposures or after the influence of toxic agents can be observed. By SEM an over-all picture of large portions of damaged organs of Corti or vestibular regions can be visualized.
In a series of micrographs it will be shown that SEM can be used as an important adjunct to other methods for the study of inner ear pathology. It is also stressed that the combined use of SEM, TEM and other techniques is necesarry for optimal results.

SCANNING ELECTRON MICROSCOPY OF THE HUMAN PLACENTA.

Fox, H. and Agrafojo, A.

Departments of pathology, University of Manchester and St. Mary's Hospital, Manchester, England.

Scanning electron microscopy confirms that the trophoblast is, in all areas, covered by microvilli. During the first trimester the microvilli tend to be ridge-shaped and are often arranged in a semi-mosaic fashion. In the mature placenta the microvilli are more digitate and less regularly arranged. As pregnancy progresses the trophoblast shows evidence of differentiation as evidenced by the appearance of easily recognisable vasculo-syncytial membranes which bulge out from the surface and over which there is a focal loss of microvilli. In prolonged pregnancy these membranes tend to disappear but the microvilli otherwise show no change.

SCANNING ELECTRON MICROSCOPE STUDIES OF SYNOVIAL TISSUE IN RHEUMATOID ARTHRITIS

D.L. Gardner.

Institute of pathology, Queen's University, Belfast, U.K.

Synovial tissue obtained at synovectomy for rheumatoid (RA) synovitis and from normal persons with injured menisci, were fixed in cold buffered glutaraldehyde, processed through acetone, air-dried and coated before examination in a Cambridge Stereoscan 2 scanning electron microscope (SEM). Three-dimensional light microscope studies of normal synovial tissue revealed an orderly pattern in which cell surfaces protruded as hexagonal arrays. From cell surfaces the SEM showed that much smaller processes projected. It is assumed that these surfaces contributed to the secretory functions of the B(F) cells and to phagocytosis by A(M) cells.

In RA the synovial surface is obscured by fibrin. Many polymorphs lie on the synovia and the delicate synovial processes are flattened and distorted to give an appearance that recalls the leaf-like form of the intestinal villi in the malabsorption syndrome. Fibrin and synovial fluid combine to give a zonal muddy appearance. The surface changes probably contribute to increased secretion of synovial fluid of low viscosity and interfere with the fibrinolysis that normally removes transuded fibrin. Thus, a vicious circle, leading to auto-allergic synovitis, is established.

SCANNING ELECTRON MICROSCOPY OF THE LUNGS

Janusz Groniowski and Michał Walski
Department of Pathological Anatomy
Medical Academy, Warsaw, Poland

Scanning electron microscopy enables one to observe the architecture of the air passages from the luminal side. Also some details of bronchiolar and alveolar relief can be observed. A simple preparatory procedure for scanning electron microscopy has been elaborated in dog lungs. Intravenously anesthetized animals were ventilated on a respirator while their chest were opened. Fragments from subpleural parts of the lungs were clamped with wooden forceps and specimens approximately 1.5 cm in diameter were removed. The clamped tissue was plunged into fixative, immediately. The specimen was fixed in 1.0% osmium tetroxide or in 3.6% glutaraldehyde /phosphate buffered at pH 7.4/ for 3 hrs. After fixation the specimen was cut into small cubes. The samples were dehydrated in a series of graded ethanol and acetone solutions and, finally, in propylene oxide. Dried samples were coated with a carbon and gold film. The specimens were studied in a JEOL scanning electron microscope JMS-2, using a beam accelerating voltage of 10 KV.

Effects of the inflation on the pulmonary parenchyma are evident. It influences greatly the diameter of the terminal air passages as well as the surface relief of the alveoli. In the collapsed lung the luminal face of alveoli revealed a very characteristic relief of plications.

SCANNING ELECTRON MICROSCOPY OF DOG THYROID SLICES

Ketelbant-Balasse, Paule
Department of Pathology, University of Brussels, Belgium

The scanning electron microscope easily provides three-dimensional pictures of thyroid vesicles. Our observations have shown, in control animals, that the apical surface of thyroid cells is covered by numerous microvilli. Shortly after TSH stimulation, newly formed large pseudopods emerge from these cells. This phenomenon is inhibited by microtubule inhibitors such as colchicine, vinca alcaloids, heavy water and cytochalasin B. In vitro, the number of pseudopods, their structure and the latency of response to different concentrations of TSH has been estimated. The structure of the apical pole of human thyroid cells in normal and pathological conditions has also been studied.

SCANNING ELECTRON MICROSCOPY OF ELASTASE EMPHYSEMA

Kuhn, Charles, Washington University, St. Louis, Mo.

Emphysema was induced in hamsters by an intratracheal injection of 25 units of porcine pancreatic elastase. Within 4 hours after injection the elastase was inactivated. By scanning electron microscopy (SEM), alveolar ducts were dilated. Fibrin strands, erythrocytes and phagocytic cells were seen in alveolar spaces Subsequently the hemorrhage and exudate resolved but abnormal air spaces continued to enlarge, at least up to two months. The abnormal air spaces formed by dilation of alveolar ducts with shortening and retraction of interalveolar septa. Interalveolar pores of Kohn were larger than in normal animals, focally increased in number and distributed irregularly.

Elastic fibers of control and elastase-injected hamster lungs were prepared for SEM by corrosion of the lungs with formic acid followed by freeze-drying. Control elastic fibers formed a continous network of branching fibers with nearly uniform diameter. After elastase injection breaks in the elastin network were abundant and the amount of elastic fiber obtained was reduced.

For comparison, specimens of early human centrolobular emphysema and congenital lobar emphysema were available. In early emphysema in adult human lungs, marked fenestration of interalveolar septa occurred without septal shortening. In congenital lobar emphysema, marked distension of alveolar ducts was accompanied by flattening of alveolar septa similar to elastase emphysema, but without abnormal fenestration.

Elastase-induced emphysema is a mixed distensive and destructive emphysema. The pathogenesis may be related in part to altered mechanical behavior of the tissue.

STUDIES ON THE STRUCTURE AND EXTENSIBILITY OF SKIN

Millington, P.F., Gibson, T., Evans, J. and Wilkinson, R.
Bioengineering Unit, University of Strathclyde, Glasgow (UK)

Mechanical properties of skin are largely determined by the composition and organisation of dermal tissues. The scanning electron microscope has enabled us to assemble a general three dimensional pattern for these tissues at different ages from birth to old age. As the person ages, so the low load extensibility of skin decreases and the arrangement of collagen bundles changes from a loose packed, twisted configuration to a more sheet like arrangement. There is, however, little change in the rupture characteristics for healthy skin.

The structure of the dermis is very variable and is not one to be described readily. There is some orientation of the fibre bundles which is reflected in the anisotropy found on most parts of the body surface. This anisotropy can be demonstrated in a number of ways, but can be shown simply by application of negative pressure over a defined area of the body surface and noting the area of the relaxed tissue. The lines linking the principal axes of the elipses so formed are also related to Langer lines.

Since large elastin bundles appear very similar to collagen bundles it is necessary to deduce which fibres are elastin by comparison with light microscope data. In any case, the two methods should be used concurrently when attempting to understand pathological conditions. An example of a case of epidermolysis bullosa will be used to illustrate the potential value of this type of information in understanding disorders of the integument.

STRUCTURE AND DIFFUSION PROPERTIES OF CARTILAGE FOLLOWING PAPAIN DIGESTION

P.F. Millington and R. Mulholland
Bioengineering Unit, University of Strathclyde, Glasgow (UK).

Since Benninghoff proposed his arcade theory (1), the detailed structure of articular cartilage has been subject to much discussion. The fibrous structure at or near the surface is important not only in its load bearing capacity but also because of its possible role in fluid movement. Using the more conventional techniques of specimen preparation for scanning microscopy including tissue fracture and peeling, we have built up a picture of the three dimensional structure of collagen near the articular surface. The parallel fibrils at the surface give way to a two dimensional network in the subjacent tissue and finally to a more random array (2,3). The studies on papain digested tissue did not conflict with these general interpretations but indicated that there may also be an arcade like arrangement from the deep zone to the surface. How much these patterns depend on drying and other artefacts is still being pursued and critical point drying techniques may give further clues.

The movement of substances by diffusion both out of and throughout the cartilage will be affected by the fibre patterns. A knowledge of diffusion rates would be important correlative information. The diffusion rate normal to the surface is said to be about $5.8 \times 10^{16} M^4/Ns$. Our measurements of diffusion parallel to the surface indicates a rate of about $3.5 \times 10^{16} M^4/Ns$. After papain digestion the lateral diffusion rate is not much different.

1. Benninghoff A., Z.Anat. Entw. Gesch 76,43 (1925)
2. Mitel, M.A. and Millington P.E., Micron 2, 236 (1971)
3. Millington, P.F. and Clarke I.C. Proc. Perspect. Biomed. Eng. 1972 (in press)

EXAMINATION OF PHAGOZYTATED SUBSTANCES IN CELLS IN SEMITHIN SECTIONS BY SCANNING ELECTRON MICROSCOPY.

Morgenroth, Konrad and Blaschke, Rochus
From the Institue of Pathology and the Institute for Medical Physics of the University in Münster.

An exact evidenee and the morphological localisation of the phagozytic substances in the macrophages, can in many cases, not be achieved with histochemical methods. The energy dispersive X-ray analysis on the semithin section in scanning transmission enables a direct analysis of phagosomes in the cell. The value of this method is demonstrated in the example of the phagosomes in alveolar macrophages in experimental silicosis of the guinea pig and in asbestosis of the human being. An exact localisation of the phagozytic substances in the cell is possible in this manner.

FUNDAMENTALS AND ADVANCES OF SCANNING ELECTRON MICROSCOPY IN DERMATOHISTOPATHOLOGY.

Orfanos, C.E., Mahrle, G., Dermat.Klin., Köln-GFR.

SCANNING-ELECTRON-MICROSCOPIC OBSERVATIONS ABOUT HERPES-INDUCED CELL SURFACE ANTIGENS AND THE ACTION OF CYTOCHALASIN B.

Richter, I.E., Just, I., Falke, D., Inst. of Path. of Bundeswehr, Mainz; Division of exp. Virology, Inst. of Med. Microbiology, University of Mainz-GFR.

Primary rabbit kidney were infected with Herpes-virus-strains /type I and II/. After various treatments the cells were fixed and finally prepared for scanning-electron-microscopy. After performance of the immun-adherance-hamadsorption test we observed connections between virus specific surface antigens and "O"-red blood cells. Herpes-induced giant cells, exhibited special surface alterations. Cytochalasin B is well known to cause retraction of the cytoplasma and extrusion of nuclei from cells in vitro. After application of Cyto B to herpes-induced giant cells no such reaction to the compound could be observed, whereas the cell-controls reacted with special morphological signs. If induced either by type I or II, they did not react after addition of Cyto B; this is true likewise of the giant cells are small or large. We conclude that a special cytopathic action of the giant cell forming virus strains upon fused cells takes place. Therefore not only the DNA-, RNA- or protein metabolism is inhibited some time after infection but there should be a special action of the virus upon the Cyto B sensitive complex.

SCANNING ELECTRON MICROSCOPY OF THE GASTROINTESTINAL TRACT

Siew, S.
University of Pittsburgh, Department of Pathology, Pittsburgh, Pa., USA

Scanning Electron Microscopy was performed on 1, Stomach: a, normal, b, non-specific acute gastritis, c, gastric ulcer 2, Duodenum: a, normal, b, duodenitis, c, duodenal ulcer 3, Jejunum: a, normal, 4, Ileum: a, normal, b, non-specific acute ileitis, c, regional ileitis 5, Colon: a, normal, b, ulcerative colitis, c, secondary megacolon, d, spastic colon (irritable bowel syndrome). The tissue was obtained by means of A-endoscopic biopsy (2b,3a,4d); B-operative resection (1a,b,c, 2a,4a,b,c 5a,b,c,; C-autopsy (fresh) 2c. All the specimens were fixed in 2.5% glutaraldehyde in phosphate buffer pH 7.4 and post-fixed in osmium tetroxide. Different techniques of specimen preparation were then compared;-propylene glycol, graded alcohols, glycerol, freeze drying, critical point drying.

Some of the more significant results in the investigation have been the demonstration by SEM of the pathogenesis of parenchymatous damage in the mucosal cells in gastritis and in relation to gastric and duodenal ulceration, which progressed from a focal denudation of microvilli to a "punched out" appearance of the cells and culminated in an extensive loss of cell structure; the development of the lesions of ulcerative colitis and the presence of mucosal edema with encroachment upon the crypts in the irritable bowel syndrome. It is concluded that scanning electron microscopy will prove to be a valuable method of investigation of gastrointestinal pathology.

CRYO-SCANNING ELECTRON MICROSCOPIC OBSERVATION OF HUMAN EPIDERMIS

Junichi TOKUNAGA
E.M.Laboratory, Department of Microbiology, Kyushu Dental College, Kitakyushu, Japan

Considerable progress has already been made in removing water from cell, formerly by the use of chemical desicants, and more recently by freezing the cell and applying freeze drying, freeze substitution and critical point drying.

A new attempt was made to bring into the SEM a cell or tissue in a frozen states (Echlin,P. 1970). This attempt proved successful in the case of the specimens of human epidermis. The specimens were taken from cadavers or living body, as biopsy material, and fixed in glutar: formaldehyde mixture solution for several days After fixation, distilled water was used to dilute electrolytes to an insignificant level before freezing. The tissue samples were plunged into Freon 22 previously maintained at its melting point by means of liquid nitrogen. The specimens were observed in the SEM equipped with a specially deviced cold stage (JEOL, SEM-U3-CRU), without any chemical treatment and coating.

Good images were obtained as the skin remained in its natural shape without exaggerated foldings and wrinkles as they occur in acetone - air - drying.

" The results will be discussed. "

ON PATHOMECHANICS OF DERMATOPHYTIC INVASION OF SKIN AND HAIRS.

Tosti,A., Villardita,S., Fazzini,M.L.
Institute of Experimental Dermatology, University School of Medicine, Palermo, Italy.

Evidence is given that in scalp ringworm mycelial hyphae bore into hair cortex individual burrows, progressing downwards and leaving astern chains of arthrospores. A timing between hair growth and downwards progression of hyphae results in a steady balance over the entire duration of the hair anagen.

A similar behaviour is shown by parasites in tinea versicolor in which dimorphism of Pityrosporum orbiculare allows a persistent colonization of the outer two thirds of the horny layer.

The in vitro invasion of horny structures by dermatophytes is shown to take place in a quite different way.

HISTOCHEMISTRY IN ROUTINE PATHOLOGY

Organized by

ROMHÁNYI, G.

Invited lecturers

AVTANDILOV
BIROV, V. V.
ENGEL-KING, W., CUNNINGHAM, G. G.
LAKE, B. D.
LILLIE, R. D.
LUKAŠ, Z., DVOŘÁK, K., DLUHOS, M.
ROMHÁNYI, G.
SOBEL, H. J.
SOLCIA, E., CAPELLA, C., VASALLO, G.
TANKA, D.
WOLMAN, M.

HISTOCHEMISTRY IN THE STUDY OF PATHOLOGIC AND NORMAL MUSCLE GROWN IN TISSUE CULTURE

Askanas, Valerie and Shafiq, S.A.
Institute for Muscle Disease
New York, U.S.A.

Histochemical analysis of human muscle biopsies has provided greatly expanded insight into the pathology of neuromuscular diseases, in regard both to muscle fiber type analysis and the alterations of staining patterns of various histochemical reactions within fibers. Tissue culture provides an opportunity to study the behavior of normal and pathologic muscle growing without influence of neural or humeral factors from the host. We have developed a method ("sandwich" technique) for more precise analysis of histochemical types of cultured muscle fibers and applied it to cultured normal animal muscle. Histochemical comparison of cultured normal versus dystrophic chicken muscle has also been accomplished. These techniques are now being applied to cultured normal versus dystrophic mouse muscle, normal rat muscle, and normal versus abnormal human muscle. The rate of growth of cultures from both dystrophic and denervated muscles was accelarated with comparison to the normal muscle culture. Electron microscopic study of this material include ferritin and calcium uptake experiments.

THE PERSPECTIVES IN MICROSPECTROPHOTOMETRIC DIAGNOSIS OF PRE-TUMOUR PROCESSES AND MALIGNANT TUMOURS

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The results of DNA microspectrophotometry application for histologic diagnosis of preblastomatoses and malignant tumours /larynx, large intestine, endometry, and nevus/ obtained in coauthorship with Kazantseva I. and Chervonnaja L. are discussed. Dynamics of DNA content changes expressed in units of ploidy were found to be the important additional diagnostic test. It is advisable to use the sign variety expressed by histograms and average values of DNA content in tissue. "The index of DNA accumulation" /arithmetic weighted mean/ demonstrating the general mass of genetic material changes is proposed. In normal epithelium this index was found to be 2,3-2,8; in benign tumours and simple hyperplasia 2,4-4,8; in atypical hyperplasia 4,9-6,5; in cancer 9,6-10,8; in primary melanoma of skin the index was 2,5 times and in metastasis 4 times as high as in nevus. The mathematical description of the process of DNA content changes and "the scale of malignization" are presented. The discovered dependence is termed as exponential low of DNA accumulation in proliferating malignizating cell populations. The first redoubling of DNA content is reflected by atypical proliferation, the second - by malignant growth.

CHARACTERIZATION OF CYTOPLASMIC DNA FROM ISOLATED HUMAN TONSILLAR CELLS

Baló-Banga, J. Mathias and Antoni, Ferenc

Cytoplasmic DNA was prepared from the separated cytoplasmic fraction of tonsillar cells using detergent Nonidet P-40, and compared with nuclear DNA of the same cells. The bulk of cytoplasmic DNA />90%/ had a buoyant density in neutral caesium chloride gradients equal with one of the two components of nuclear DNA.

Comparisons of nuclear and cytoplasmic DNA on caesium chloride ethidium-bromide gradients had excluded the presence of covalently closed circular DNA, contaminating to significant amounts.

Further comparisons of the two DNA specimens were carried out using alkaline sucrose velocity sedimentation and analysis of thermal hyperchromicity effect.

The sedimentation patterns of radioactively labelled total cellular DNA have revealed the labelling of the same DNA component within the nuclei that was found after cellular fractionation in the cytoplasms of the tonsillar cells.

A possible pathognomic role of the characterized tonsillar-cell cytoplasmic-DNA concerning secondary rheumatoid diseases and autoimmune reactions is taken in account.

THE CONTRIBUTION OF SOME HISTOCHEMICAL METHODS IN THE DIAGNOSIS OF BREAST CANCER.

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The histochemical methods used in the breast cancer diagnosis in routine practice are presented.

Among these the techniques for the detection of acid and neutral M.P.Z., as well as the silver impregnations for reticulin fibres and selective stainings for amyloid were the most useful.

The correlations between various morphological forms of breast cancers and changes of stromal components in neoplastic zone and in surrounding tissues, before and after irradiation are pointed out.

The following of basement membrane integrity, of M.P.Z. depolymerization stages as well as the detection of amyloid deposits or of hyaline evolution in stroma are considered as valuable morphological criteria with a prognostic significance.

THE IMPORTANCE OF HISTOCHEMISTRY IN PATHOLOGY.

Birov,V.V., Laboratory of Morphology, Chervonograd-USSR.

As a result of introduction of the methods of histochemistry a considerable progress has been made in the understanding of the pathomechanism of many human pathological conditions. The specific histochemical demonstration of certain substances as well as the histoenzymatic reactions made possible the clear-cut identification of certain cell types,the rapid and efficient diagnosis of blastomic proliferations and of changes in the parenchymal and/or interstitial tissue elements at the resolution level of light microscopy.

without the use of carefully standardized and scrupulously evaluated histochemical studies we were not able to study in detail the metabolic processes of the different cells under normal or pathological conditions /functional histochemistry/ nor the effect and made of action of different drugs /metabolic regulation-drug control/.

Histochemistry and electron microscopy applied to animal experiments as models offer us a tool to learn more about the molecular mechanisms involved in pathological changes in humans and opens up new possibilities for more efficient therapy.

APPLIED HISTOCHEMISTRY OF THE GASTRIC MUCOSA'S CELL POPULATION.

V.V.Birov, Ja.N.Panasiuk, E.A.Gehnyer, Laboratory of Morphology, Cservonograd, USSR.

In patients with chronic gastritis or peptic ulcer we exami ed histochemically and spectrocytophotometrically the differences in the activity and localization of the glycolytic; and glycogenolytic enzymes, pentose and 1-glycerol-3-phosphate shunts, tricarbonic acid and xylose-uric acid cycles electron-transport systems, ATPase and of the lysosomal hydrolases.

In the hydrochloric acid producing cells an exalted activity was found of the glycolitic enzymes, the tricarbonic acid cycle and of all enzymes of the electron-transport system. There were also demonstrable all morphological signs /in the ergastoplasm, mitochondria, nuclei and other organelles/ of an increased consumption of the cell's energy sources required for the synthesis of ATP and other macroerg compounds and for the production of HCl.

In different forms of chronic gastritis the appearence of intestinal epithelium was observed in the stomach.These enterocytes had histochemical characteristics,similar to those found at the normal transition zones of gastric to intestinal mucosa.They exhibited, however,in the reparative areas some characteristic changes in their regulation mechanismus.

DNA-SYNTHESIS IN 14-DAYS AGED RAT EMBRYONS FROM MOTHERS TREATED WITH FOZALON IN ADVANCE.

Burkova,T., Vachkova,R., Mihailova,Z., Center of Hygiene, Dept.of Pathology, Sofia-Bulgaria.

The authors followed up under the conditions of a chronic experiment the alterations in the parameters of DNA-synthesis in the liver of rats' embryons who'se mothers had been treated with 1/10 and 1/20 DL Fozalon before and during their pregnancy. As a result from the autoradiographic,histochemical and morphologic studies,which has been carried out, the authors established,that in the liver of the test animals /mothers/ changes appeared and namely chronical hepatite,accompained by a compensatory raised activity of some mitochondrial and oxidative-reducible ferments /AP, AcP,SDH,LDH/ and an accelerated DNA synthesis.

At the same time the period T/the time of a DNA cycle/ in rat embryons is shorter,then that one of the control embryo,and mainly, during the presynthetic phase /G_1/and t/M+G_2

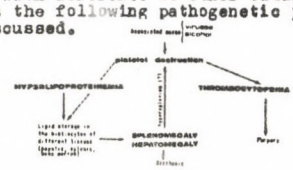
The authors supposed,that the changes in the cycle of DNA are due to the stimulating effect of the eliminated from the mothers liver tissue "growth hormones" during the processes of regeneration.

The direct effect of Fozalon on the rat's embryons is less possible,because the transplacentar passage of this pesticide has not been confermed yet.

HYPERLIPOPROTEINEMIA AND THE SYNDROME OF THE SEA-BLUE HISTIOCITE.

Castoldi,G.L., Grusovin,G.D., Scapoli,G.L., Dept.of Internal Medicine,University of Ferrara, Ferrara-Italy.

The presence in the spleen and bone marrow of histiocytes containing bluish stained granules /Pappenheim's preparations/ has been considered a rinding common to several lipid storage disorders,both congenital and acquired.Hyperlipoproteinemia is one of the conditions occasionally found to be associated with the presence of these cells. Here is presented a case of a 34 y.old woman with familial hyperlipoproteinemia,who showed mild thrombocytopenia,spleen enlargement, liver cirrhosis, lung infiltratos,and blue histiocytes in the marrow. Cytochemical studies of these cells were consistent with the presence in their cytoplasm of lipofuscin/ceroid type/. All together these features are reminiscent of a peculiar form of ceroid histiocytosis described by Silverstein et al. as "the syndrome of the sea-blue histiocyte". With reference to other similar conditions the following pathogenetic patterns are discussed.



THE EFFECT OF THE IRON AND COPPER IONS UPON FIBRILOGENESIS.

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Bucharest - Romania

The effect of the iron and copper ions upon fibrilogenesis by means of hystological methods was studied.

The enzymes of the Krebs cycle, of the anaerobic glycolysis, of the pentose shunt, the dysphorases, the ATP-ases, the prolin-oxidase and of hydroxiprolin-epimerase was investigated in derm.

Some significant methabolic transformations in the conjunctive cells were detected in sideropeny as in siderose and hypercupremie.

Prolin-oxidase activity increase in siderose and hydroxiprolin-epimerase activity increase in hypercupremia.

ULTRASTRUCTURE OF BASEMENT MEMBRANE COMPONENTS AS REVEALED BY TOPO-OPTICAL REACTIONS

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Basement membranes show no structural organization in electron microscope, but topo-optical reactions indicate that they are composed of longitudinally arranged collagen-protein/phenol reaction/ and transversally oriented lipids /as shown by their negative intrinsic birefringence/. The ultrastructure of the carbohydrate components, however, has not been successfully investigated so far.

In the present investigations topo-optical reactions were used to demonstrate the ultrastructural organization of the carbohydrate components of the basement membranes. It was found tha selective sulfation of the vicinal OH-groups resulted in oriented dye binding with metachromasia and strong negative birefringence indicating a linear arrangement of the vicinal OH-groups of the carbohydrate components parallel to the micellar texture of basement membrane proteins.

After blocking of the vicinal OH-groups by periodic acid a selective topo-optical staining reaction of collagen is achieved as a result of sulfate esterification of the OH-proline groups of collagen. In this way a selective qualitative and quantitative analysis of collagen and carbohydrate components in the basement membranes became possible.

ACID MUCOPOLYSACCHARIDES AND INFLAMMATORY DISEASE

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For the morphological examination of the chronic inflammated tissue - especially at biopsy material - the demonstration of acid mucopolysaccharides can be of advantage in double respect: Firstly these diffuse localized substances of the florid chronic inflammation can also appear in such tissue areas, at which under usual routine dyings no signs of an florid process appear. Secondly at the repeated proof of acid mucopolysaccharides is, prognostically seen, a progredient increase of fibrosis of the concerned organs is to be expected. At the acute inflammation the perivasal occurrence of acid mucopolysaccharides indicates an early phase of exudation. As for the routine use for the demonstration of acid mucopolysaccharides the simple " Alcianblau - Kernechtrot " staining method is to be recommended.

HISTOCHEMISTRY IN NEUROMUSCULAR DISEASE (NMD)PATHOLOGY

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Histochemical (HC) analysis of fresh-frozen sections is necessary in routine analysis of muscle tissue in human NMDs and animal models. Paraffin sections are inadequate to diagnose HC different normal muscle fibe-types and selective involvement of one type in certain NMDs; e.g., type II fiber atrophy (cachexia, distant cancer, corticosteroid atrophy); the disease type-I-fiber-hypotrophy-with central nuclei; and type I fiber predominance in central core disease, congenital rod (nemaline) disease, and some cases of benign congenita hypotonia. Paraffin sections do not allow diagnosis of HC identifiable: type-grouping (chronic denervation with collateral re-innervation); scattered small angular DPNH-TR-dark and esterase-dark fibers of minimal denervation; subtle "myopathic" changes of alkaline-phosphatase-positive fibers; "ragged-red" fibers (with succinate-dehydrogenase-rich collections of abnormal mitochondria) characteristic of some progressive ophthalmoplegias and rare other disorders; tubular aggregates; densely acid-phosphatase-positive fibers of acid maltase deficiency; and phosphorylase deficiency. HC of fresh-frozen muscle sections displays more lucidly: changes of ordinary denervation and myopathy (including grouping pattern of abnormal fibers in Duchenne muscular dystrophy); rods (modified trichrome); central cores and targets (DPNH-TR); amyloid (crystal violet metachromasia, PAS+); thionin-metachromatic material in intramuscular nerves of leucodystrophy; atypical PAS+ material in a rare cardio-skeletal myopathy; and glycolipoprotein (PAS and sudan-black+) of vessels of Fabry's disease. Fresh-frozen sections and HC are quick - 1 hour total.

HISTOMORPHOLOGICAL CHANGES OF THE LIVER AND SERUM GLYCOPROTEID CONCENTRATIONS IN CHRONIC LIVER DISEASES

Fehér, János; Jakab, Lajos; Szilvási, István and Józsa, László
Semmelweis University of Medicine. 3rd Dept. of Medicine, National Institute of Traumatology.
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The concentration of the serum immunglobulins - IgG, IgA and IgM - and that of the serum coeruloplasmin, alpha-2-macroglobulin, beta-1-C-globulin and transferrin were determined from patients with chronic hepatitis, by radial immundiffusion methods. In addition the behaviour of the humoral antibodies against to the antigen fractions originating from allogen liver nucleus, mitochondrium and soluble protein were studied by passive haemagglutination methods. A correlation was found between the histomorphological changes of the liver and the glycoproteid concentrations of the serum. In chronic persistent hepatitis the concentration of the IgM in chronic aggressive hepatitis that of the three immunglobulins was significantly higher than the normal value. The level of coeruloplasmin and alpha-2-macroglobulin was parallely increased to the severity of the inflammatory mesenchymal reaction. The concentration of beta-1-C-globulin and transferrin was practically unchanged.

PROGNOSTICAL VALUE OF HISTOCHEMICAL INVESTIGATION OF LIVER BIOPSIES IN LIVER DISEASES

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The authors investigated with histochemical methods the alcaline and acid phosphatase, lipase and the mucopolysaccharides of the liver tissue, obtained by needle biopsy from 200 patients with acute and chronic hepatitis, cirrhosis, hepatic atrophy and chronic cholecystopathies. This examination visualizes the evolution of the morphofunctional state of the lesions of biliar capillaries, of the Kupffer cells and of the conjunctive tissue. Repeated biopsies revealed that the extracellular appearance of the alcaline phosphatase activity in the periportal spaces or between the trabeculas as well as the deposition of acid mucopolysaccharides, represent early signes of recent fibrogenesis and its evolution into fibrosis or cirrhosis. During recovery, the modified histochemical picture returns to the normal, while its persistence indicate the evolutive tendence of the disease. At the beginning of the necrosis of liver cells, the activity of acid phosphatase increases, dissappearing later on.

The histochemical study supplies useful data not only regarding the functional state of the liver parenchyma and the exact diagnosis, but since it indicates the evolution of the pathologic processes earlier as the current methods, it must be considered more valuable in the prognostical evaluation of liver diseases.

HISTOCHEMICAL ASPECTS CONCERNING THE ROLE OF INTRACELLULAR PROTEASES IN PATHOLOGY.

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The pathogenetic and diagnostic significance of the protease enzymehistochemistry is emphasised as a consequence of the results obtained by a histochemical analysis of catepsin D, tryptase, catepsin C and aryl amidase activities in stress and chronic degenerative diseases with an immuna mechanism /EAE, chronic active hepatitis, skin graft rejection/.

A complex and differential participation of these enzymes is prouved to be present in the genesis of autolitic lesions in the nervous system during stress, at the same time with alteration of lysosomal permeability. In the context of the immunological agression, an enhanced activity of proteases, provided by the activated satellite lymph nodes is implicated in the afferent inductive mechanism of immunogenesis. In the target tissues /nervous system, liver, skin/ histochemical behaviour of proteases suggests their role as mediators and final effectors in the sequence of immunological phenomena, leading to autolitic and heterolitic lesions.

ENZYME HISTOCHEMISTRY IN ROUTINE ORAL HISTOPATHOLOGY.

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A new routine will be demonstrated which enables an exploitation of tissue biopsies, aimed at diagnosis, also for histochemical analyses for studies on pathogenesis and visualization of enzyme characteristics of different pathological conditions for the students. Cold microtome methods are used instead of paraffin embedding. The biopsies are transported from the operation theatre to the Laboratory in cold ($+4^{\circ}C$) HISTOCON (Bethlehem Trading AB, Sweden). Freezing of the tissues is then performed within 48 hours after the surgical excision. These simple procedures have been found to preserve both morphological and histochemical characteristics comparable to fresh frozen controls (Heyden et al., J. oral Path. 1: 12-21, 1972). The standardized transports also facilitate standardized histological, chemical component histochemical and enzyme histochemical analyses to be performed on each specimen. A strict standardisation is necessary for comparative studies. Data on, i.a., the activities of diaphorases, dehydrogenases, acid phosphatases, alkaline phosphatases and proteases in different diseases have accumulated at the prospect of finding more criteria to be utilized in future differential diagnostic work - especially when dealing with, i.a. oral "white lesions".

ENZYME-HISTOCHEMICAL AND BIOCHEMICAL ASPECTS OF LIVER DAMAGE CAUSED BY LANTHANUM TRICHLORIDE

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Department of Pathology, County Hospital Pécs, Department of Pathology, National Institute of Rheumatism and Physiotherapy, Budapest, and Department of Clinical Chemistry, Medical University Pécs, Hungary.

The livers of rats treated with lanthanum (La) trichloride (2.4 mg/100 g b.w.) initially showed transient degenerative-regressive cellular damage accompanied by a decrease in activity of the hydrolytic enzymes of the liver. The decrease was confined chiefly to the periphery of the lobules. In response to a dose of 4.8 mg/100 g b.w. there was centrolobular necrobiotic transformation associated with the disappearance of glycogen and loss of activity of phosphorylase as well as of oxidative enzymes.

The activity values of the liver homogenates were in agreement with the histochemical pattern.

The present data provide a better insight into the mechanism of the damage caused by La.

DEVELOPMENT OF EXPERIMENTAL ARTHRITIS IN ULTRASOUND-TREATED ANIMALS

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National Institute of Rheumatism and Physiotherapy, Department of Morphology, Laboratory of Histochemistry, Budapest, Hungary

The effect of ultrasound on the arthritis induced by the granuloma pouch method has been studied with enzyme histochemical methods.

According to the observations made, treatment with ultrasound after the induction of arthritis temporarily diminished periarticular edema and inactivated lysosomal reactions. When treatment with ultrasound is carried out before induction of arthritis, both the oxidative and the lysosomal activities are increased. On the 10th day of observation there is no substantial difference, either morphological or histochemical, between the differently treated groups.

HISTOCHEMICAL DIFFERENTIATION OF MUCOSUBSTANCES IN MESENCHYMAL TUMOURS.

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Department of Pathology, University of Gothenburg and Department of Pathology, University of Linköping, Sweden.

Differentiation of acid mucopolysaccharides in connective tissue has been accomplished by Scott et al. utilising the critical electrolyte concentration phenomenon. Alcan blue stains the known mucopolysaccharides up to a critical ionic strength ($MgCl_2$ solution), varying for the different mucopolysaccharides. The authors have used this method for histochemical differentiation of the mucopolysaccharides in myxoid and chondroid tumours, and chordomas. Tissue controls with biochemically characterised mucopolysaccharides were used (ganglion, fetal and adult cartilage, mast cells, nucleus pulposus and cock's comb). Some 80 bone and soft tissue tumours were examined. The mucosubstance in myxoma and myxoid liposarcoma stained up to the same critical electrolyte concentration as the control tissue containing hyaluronic acid; chondromatosis in bursa, tendon and synovia and well differentiated chondrosarcoma showed the same staining pattern as keratan sulfate in adult cartilage; low differentiated chondrosarcoma and extraskeletal and mesenchymal chondrosarcoma stained as fetal cartilage containing chondroitin sulfate. The mucosubstance in chordoma stained as notochordal tissue (keratan sulfate) in nucleus pulposus, which gives support for the opinion that chordoma takes origin from ectopic notochordal tissue. The potential value of histochemical methods in the typing of bone and soft tissue tumours is stressed.

ENZYME-HISTOCHEMICAL METHODS IN HEPATOLOGY

Krustev, L., Borov, B., Popov, A.

Department of Pathology, Center of Hygiene Sofia, Bulgaria

Enzyme-histochemical methods give the possibility of finding early changes in the liver tissue, and at the same time connecting data concerning structure with function.

In the paper are discussed enzyme-histochemical methods dealing mainly with two groups of cell organelles. Those are the membrane enzymes (of the bile capillaries, as well as the sinusoids) and the lysosomal enzymes. The investigation has been carried on liver biopsies of more 400 patients with: different forms of chronic hepatitis and cirrhosis, primary and metastatic carcinoma of the liver, benign hyperbilirubinemias, various forms of cholestasis, fatty liver, hemochromatosis and hepato-lenticular degeneration.

The results are not pathognomic for the particular diseases. At the same time it is pointed towards the emerging of several "enzyme syndroms", which have diagnostic values. Some examples are the activation of alcaline phosphatase with inflammation, the inhibition of the activity of the phosphatases in neoplastic processes, the increase of lipase and esterase in the regenerating lobules, etc.

The data are discussed in connection with results of other authors as well as in the ligth of general pathology.

HISTOCHEMISTRY OF GLYCOGEN STORAGE DISEASE

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For the histochemical study of GSD fresh frozen tissue is essential. The use of formalin fixed paraffin sections does not give any useful information. Glycogen is best demonstrated by the PAS technique after coating the cut section with celloidin. Digestion with saliva is adequate to differentiate Type IV GSD from other types. Glucose -6- phosphatase activity is reliably demonstrated, and Type I GSD can be confidently diagnosed by histochemistry alone. The method for demonstration of phosphorylase activity is not entirely reliable and it may not be possible to differentiate between Types III and VI using histochemically demonstrated phosphorylase activity. A new modification for phosphorylase activity using amylose as acceptor may prove more reliable. Blood films can be used for the demonstration of excess glycogen in lymphocytes from patients with Type II GSD. Biochemical assays are nearly always necessary for confirmation of the types of GSD.

Lake B. D. (1970) Histochem. J. 2 441-450

The Periodic Acid Schiff Reaction in Diagnostic Pathology. R. D. Lillie, Department of Pathology, LSU Medical Center, New Orleans, La., USA.

Carcinoma mucins agree in several reactions with those of the tissue of origin. Mucoscirrhus gastric carcinoma was now readily diagnosed. Renal glomerular stroma was sharply shown. Globular red bodies appeared in diabetic kidneys, ingrowth of collagen in glomerular scarring shown by the allochrome variant all proved of diagnostic value. Allochrome: a picromethyl blue used after PAS, and collagen changes color from red to blue, basement membranes remain red PAS has largely replaced carmine methods for glycogen and epithelial mucins. The coarsely granular glycogen in neutrophil leucocytes in acute inflammation, in blood smears and in tissue is of definite diagnostic value Entamoeba histolytica in tissue is more conspicuous by its granular glycogen. α-Amylase digestion confirms identity as glycogen. β-Amylase digests starch but not glycogen. Starch has been found in actinomycotic sinus tracts connecting with the intestine. The PAS and the Bauer are useful in finding fungi (Histoplasma) in lesions. Substitution of Grocott's methenamine silver for Schiff is better in fungus recognition. Use of a m-aminophenol, fast black K sequence in place of Schiff is useful for fungi and with HIO_4 yields a stroma demonstration more complete than with silver reticulum variants, showing smooth muscle stroma. PAS before Perls ferrocyanide reaction shows relation of iron to mucins and stroma. Combination of PAS with Alcian blue, Astrablau and Hale's reaction to characterize mucins, is useful on muciparous tumors of uncertain organ origin.

ON ARGENTAFFIN CELLS IN THYROID AND PARATHYROID GLANDS

Ljungberg, Otto and Nowak, Krystyna

University Department of Pathology, General Hospital, Malmö, Sweden and Department of Pathological Anatomy, Krakow, Poland.

Argentaffin cells in the thyroid and parathyroid glands have been demonstrated in cases of medullary carcinoma. In addition, cells with identical characteristics have easily been found in patients with hyperparathyroidism, but only occasionally in cases of thyroid neoplasms other than medullary carcinoma, various benign thyroid diseases and in normal glands.
Their morphological, topographical and histochemical characteristics are distinct from those of the calcitonin cells (C-cells).

LYSOSOMAL HYDROLASES IN DYSTROPHIC MUSCLES.

Lukáš, Zdeněk, Dvořák, Karel and Dluhoš, Max, Ind. Department of Pathology, Children s Hospital, Brno, ČSSR.

We will report about the first results of our histological, histochemical and electrn microscopic examination of 62 muscle biopsies of 58 men.

By using of the azo-dye methods to demonstration of acid phosphatase (AcP), non specific esterase (NE), beta-glucuronidase (GU), N-acetyl-beta glucosaminidase (GA), the granular reaction product can be observed both in normal and diseased muscles.

1) The number of lysosomal hydrolases in granular localization in normal muscles is sparse.

2) In denervation atrophy their number increases, before all in the atrophic fibres. The concentration of the granules, however, exceeds not the normal variation in some cases.

3) The most pronounced accumulation of granules can be observed in dystrophic muscles particularly in case of collagenous diseases.

The most part of granules is localized beneath the sarcolemma. Their high activity of NE is constant, while the reaction intensity of AcP, GU and GA varies in some cases. Most of them exhibit the well developped autofluorescence. Their ultrastructure presents various degrees of formation the residual bodies with lipofuscin.

HISTOCHEMICAL FINDINGS IN ATYPICAL EPITHELIAL HYPERPLASIA ASSOCIATED WITH BREAST CANCER AND FIBROCYSTIC DISEASE

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Investigations on the presence, localization and intensity of PAS reaction, alkaline and acid phosphatase activity in breast tumor tissue of female patients were undertaken. The results of a correlation of histochemical findings obtained in different histomorphological features of breast tumor tissue including also the surrounding breast parenchyma might be of interest on possible significant histochemical findings in atypical epithelial hyperplasia with respect to the development of breast cancer. Histochemical findings could help in routine diagnosis of breast tumor tissue as to more precise evaluation of its character.

HISTOENZYMOLOGICAL ASPECTS OF DIHYDROFOLATE REDUCTASE ACTIVITY IN NORMAL AND LEUKEMIC BLOOD "IN VIVO".

Onicescu, Doina and Tasca, Luminita
Faculty of Medicine, Dept. of Histology Bucharest, Romania.

By means of an original histochemical method the dihydrofolate reductase activity was studied in smears of normal and chronic leukemia blood. The enzyme activity was weakly positive or negative in normal leukocytes and strongly positive in leukemic not fully differentiated leukocytes. After the beginning of chemotherapia the enzyme activity was strong in differentiated leukocytes (neutrophils, eosinophils) and negative in undifferentiated white cells. The biochemical demonstration of dihydrofolate reductase activity could be a useful method for precocious diagnosis of leukemia.

CYTO-ENZYMO-CHEMICAL CHANGES IN TREATED ACUTE LEUKEMIA

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The medullo-sanguine blastic population was studied in a group of 52 patients with various forms of acute leukemia. Identification of the cytologic type was made on the basis of cytochemical and cytoenzymatic criteria. The methodology used for the study of glycogen, lipids, nucleolar RNA, peroxidases, leukocytic alkaline phosphatases, muramidase, nonspecific esterases and specific esterase of the monocyte was the commonly used methodology. The patients received a therapy adapted to the cytologic type of leukemia, which consisted of an association of cytostatic drugs : Vincristin, Cerubidin, Methotrexat, Purinetol, Cytosin-Arabinosid, Endoxan, L-Asparaginase. The cyto-enzymochemical effects induced by the cytostatics were followed up dynamically both at the end of each therapy and in various periods of evolution of the disease. The results of these studies may be of theoretical significance, they contributing to the knowledge of the blastic cell metabolism, and of practical importance in concerns following up of the effects of the applied therapy and estimation of the sensitivity or resistance of the respective cells to the applied therapy.

TOPO-OPTICAL REACTIONS IN HISTOCHEMISTRY

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Topo-optical reactions /TR/ are induced on micellar textures by orientated binding of dye molecules or colorless compounds. Their usefulness is evidenced by the strong increase in the originally weak or masked birefringence of the micellar texture /with additive or inversive character/.

Since TR-s depend on the chemical - ultrastructural organization of micellar textures as well as on the molecular structure of the reactive compounds /dye/ they often have the significance of selective histochemical reactions and provide possibility for quantitative histochemical structural analysis. The TR-s significant for connective tissue structures will be discussed:

The phenol reaction /Ebner/ as a prototype of collagen specific TR, the aniline reaction of vascular elastic fibres which selectively demonstrates the elastic fibers by negative birefringence indicating their fibrillary ultrastructure, later recognized by electron microscopy; the collagen specific inversive topo-optical Congo red reaction indicating the specific charge distribution on the surface of collagen not shared by any other fibrillary components in the tissues, which provides a new possibility for definitive differentiation in the polarisation microscope between collagen with an inversive and amyloid with an additive Congo red reaction.

The ultrastructure of acetyl-collagen and sulfate-collagen associated with selective collagenolysis as revealed by specific TR-s are discussed.

THE VALUE OF HISTOCHEMICAL INVESTIGATION OF MUCOPOLYSACCHARIDES IN THE DIAGNOSIS OF HYPERTHYREOIDISM. Felicia Schneider, Lab. of Hist Ti isoara -Romania.

Histochemical studies of mucopolysaccharides were performed on intraoperatively removed thyroid gland from female patients with a clinical diagnosis of Basedow's disease. The morpho-functional condition of the gland was estimated by corroborating the histological and histochemical interrelationships between parenchyma and stroma, this permitting to establish the developmental stage of the disease. In Basedow's disease, follicular polymorphism with epithelial hyperplasia and papillary proliferation associated with the active resorption of colloid, intensification of the PAS-reactive border of thyrocytes and the increased globule contents in the supranuclear cytoplasm, reflect a secretory hyperactivity, the process of endocytosis being predominant. The stroma with its structural elements, basal membranes and basic substance implied in the plasticity of selective permeability by the depolymerization of mucopolysaccharides, is adapted to the exaggerated functional stress of the parenchyma. In advanced Basedow's disease, the involutive stage, the atrophic follicles with gradual regression of the epithelium, manifest themselves by polymerizing the glycoprotein-acid MPZ complex in the accumulated colloid. Reactive stroma becomes more abundant and exhibits gradual polymerization of the mucopolysaccharides in the basal membranes and the basic substance which reflects the irreversible involution of the parenchyma.

THE IMPORTANCE OF ENZYME HISTOCHEMICAL METHODS IN JUDGEMENT OF THE REGIONAL EFFECTS OF EXPERIMENTAL BRAIN LESIONS

Skaliczki, József; Sztriha, László and Bara, Dénes
Department of Pathology, University of Medicine, Szeged, Hungary

The histochemical reaction of the succinic dehydrogenase, lactic acid dehydrogenase, glucose-6-phosphate dehydrogenase and TPN-diaphorase enzymes was studied after electrolytic brain lesions situated in frontal planes throughout the hypothalamus of albino rats. In the damaged area the neuronal enzymic activity disappears. However, the neuroglial reaction is well demonstrable by suitable methods. The activity of the respiratory enzymes, that is vitality of the habenular and various hypothalamic nuclei partially involved in or being close to the lesion may be decreased, normal or increased. After unilateral destruction of the postcommissural fornix the enzymic activity of the ipsilateral half of the mamillary body decreases considerably.

ENZYME HISTOCHEMISTRY FOR THE PATHOLOGIST

Sobel, Harold John
Beth Israel Hospital, Max Wachstein Research Laboratories, Passaic, N. J., U.S.A.

A simple method for the histochemical visualization of cell organelles using enzyme cytochemical procedures will be presented. Most of the procedures utilized can be performed on simple frozen sections of formalin-fixed material. A few require cryostat sections.

With these procedures each of the cell organelles can be localized with the light microscope and characterized as to size, shape, number, and distribution within the cell. An evaluation can be made as to enzymic activity of each organelle as well. Many more cells can be studied with these procedures than with the electron microscope.

Various physiologic and pathologic states will be used to illustrate the value of these procedures. Electron histochemical preparations will be presented confirming the observations made with the light microscope.

DIAGNOSIS OF ENDOCRINE TUMOURS BASED ON THE HISTOCHEMISTRY AND ULTRASTRUCTURE OF THEIR SECRETORY GRANULES.

Solcia, E., Capella, C., Vassallo, G., Inst. of Path. Anat., University of Pavia, Pavia - Italy.

SOME HISTOENZYMOLOGICAL FINDINGS CONCERNING THE REGENERATION OF THE STRIATED MUSCLE FIBERS

Ştefănescu Victoria & Hagi-Paraschiv Ardeal

Department of Histology, Faculty of Medicine, Bucharest, Romania.

In order to investigate the phenomenon of regeneration a linear series of punctures were practiced in the pectoral muscle of pigeons by means of a syringe needle. Fragments were gathered at intervals of 2-12 days.

The presence of the activity of succindehydrodiagenase, lacticodehydrogenase and ATP-ase at pH 9,4 at the level of the sarcoplasms of the striated muscular fiber partially injured, pleads for the activity of the sarcoplasms at the level of which the myoblasts which determine the regeneration of the striated muscular fiber differenciate.

The sarcolema remains unharmed throughout the various stages of disorganization of the striated muscle fibers, while the conjunctive tissue of the traumatic focus plays an auxilliary part in the regeneration process (purging of the focus, limitation and trophycity of the new formed muscular tubes).

OXYDATIVE METABOLISM OF RHEUMATOID NODULE. An bio- and histochemical study.

Tanka, D.

National Institute of Rheumatism and Physiotherapy, Department of Morphology, Laboratory of Histochemistry, Budapest, Hungary

In the rheumatic nodules obtained from rheumatoid arthritis patients such enzyme histochemical phenomena could be detected as do not occur in any other chronic disease producing granulation. It is believed that further investigations concerned with the rheumatoid nodule cells different in SDH activity and in ubiquinone contents may bring us nearer to the elucidation of the pathomechanism of rheumatoid arthritis.

Electrophoretic studies prove that there is just one SDH fraction, moving with ubiquinone, in the rheumatic nodule. On extracting ubiquinone it was conspicuous that as compared for example to the rheumatoid arthritic synovia a substantially higher reducible component could be demonstrated.

HISTOENZYMOLOGICAL ASPECTS OF DIHYDROFOLATE REDUCTASE ACTIVITY IN LEUKEMIC LEUKOCYTES " IN VITRO".

Tasca, Luminita and Onicescu, Doina

Faculty of Medicine, Dept. of Histology, Bucharest, Romania.

The differentiation of the chronic myelocytic bone marrow cells and peripheral white blood cells grown "in vitro" on feeder-layers was studied by means of histochemical demonstration of dihydrofolate reductase activity. The early both medullary and peripheral cultures had morphologically and cytoenzymically much in commun with each other, showing blastoid aspects and intense enzyme activity. The 14 days-cultured cells were either morphologically or enzymically differentiated and alike with normal white blood cells, t.i. neutrophils, eosinophils and monocytoid cells.

THERAPEUTIC EFFECT OF ATP ON THE FINE STRUCTURE OF THE MYOCARDIUM DURING GENERAL HYPOXIA

Tsagareli Z.G., Jandieri K.N., Kurnosenko M.A.

Institut of Experimental Morphology, Department of Cytology, Tbilisi, USSR

In undertaking the present experiments we proceeded from the fact that the power deficit resulting from the increased demands in energy, as well as a decreased efficiency of energoformation are responsible for the myocardial changes. Effect of definite doses of ATP, introduced daily prior to the experiment, on the ultrastructural changes has been studied. The experiments have been carried out on male rats weighing 180-200 g. The subjects were divided into two groups. The first group comprised the subjects being in a state of hypoxia. The second group received an additional dose of ATP. Electron microscopic investigation of myocardium of the second group demonstrated less pronounced destructive changes, as compared with the subjects of the first group whose myocardium showed a vast site of myomolation.

INDICATION OF FUCHSINOPHILIC DEGENERATION IN DETECTION OF CARDIAC AND SKELETAL MUSCULAR FIBER LESIONS.

Wassermap,L.,Dobrescu Gioconda, Bendescu Maria, Miron Eugenia, Dept.of Pathology, Medical School, Iasy-Romania.

The authors attempted a systematic study on experimental and human materials in order to determine the indications which may give the fuchsinophilic degeneration for the appreciation of the lesions of the cardiac and skeletal muscular fiber in anatomo-pathological practice. The materials for research into myocardic fibers were obtained from: 1/ experimental cardiopathies by corticoids and Na phosphate; 2/ experimental cardiopathies following the hypervitaminosis D_2; 3/ human ischemic cardiopathies /myocardial infarct, myocardiosclerosis/; 4/ myocardiopathies in the children following interstitial pneumonia. The study of skeletal muscular fiber lesions dealt with: experimental myopathies by Coxsachie,human myopathies following the infections by Coxsachie,ocular myopathies, Steinert myopathies, myopathies of collagen diseases. Light-, fluorescence-, phase contrast microscope as well as histochemical and autoradiographic /S^{35} and Ca^{45}/ investigations revealed that the fuchsinophilic material corresponds to some alterations of muscular fibers,persisting for a relative long time. The degenerative process also affects the muscular fibers involved in the scarring process.

HISTOCHEMISTRY OF LIPID STORAGE DISEASES

Volman, Moshe

Department of Pathology, Tel-Aviv University Medical School, Ch. Sheba Medical Center, Tel-Hashomer, Israel

The histochemical approach can allow exact diagnosis of some lipidoses. This is possible when the enzyme defect is known and can be histochemically visualized or when the same is true for the stored lipid. Difficulties are caused by the fact that more than one substance is stored (for example in the (Niemann-Pick disease), through our ignorance regarding the stored material, and also because of changes which the stored material undergoes with time.

Two relevant examples are: 1. Batten's disease, in which the stored neuronal material is a chromolipid. It is suggested that the pathogenetically important constituent of the pigment is the oxidation - or polymerization catalyst rather than the lipid itself. 2. Xanthomata in which the histochemical differentiation between hyperlipemia and hypercholesterolemia is often hampered by changes with time.

PATHOLOGY OF CHROMOSOMES

Organized by

GIORDANO, A.

Invited lecturers

CZEIZEL, A., RUZICSKA, P.
FORD, Ch. E.
GIORDANO, A., CAVEZZI, A.
GROPP, A.
de GROUCHY, J.
LINDSTEN, J.
SELYEI, M.

The GENETICAL AND MORPHOLOGICAL EXAMINATION OF MALE INFERTILITY IN TESTICULAR BIOPSY

Brasch, János and László, János

Postgraduate Medical School, Dept.of Urology and Dept. of Obst.& Gynec.

Budapest, Hungary

We have carried out testicular biopsy at infertile male discovered at the andrological outpatient care off our Family Planing Service. We have carried out the histological examination and the meiotic analysis of spermatogonium. We took together the data of histological features and meiotic abnormalities and chiasma frequency. We summerise these data, that help to understand the pathogenesis of male infetility.

MALIGNANT RECIPROCAL TRANSLOCATIONS.

A.Czeizel and F.Rusicska

National Institute of Public Health, Budapest.

The rist /fetal death and severe multiple congenital malformations/ of the offspring of persons carrying balanced reciprocal translocations is as high as about 50%. In certain cases, fetal damages may develop with an even higher frequency as proven by the four cases presented: I./ TE280840; 46,XY, t/Dp+;18q-/, 4 failed pregnancies /2 spontaneous abortions one with multiple malformations, 2 still births/ II./ SLO21139 46,XX/Cp+;Cq-/, 5 failed pregnancies /live births with multiple malformations/; III./ JBs120136, 46,XY/46,XY, t/Cq-,+?/, 13 spontaneous abortions; IV./ JF042546, 46,XX t/Cp-,+?/ 3 failed pregnancies /1 spontaneous abortions, 1 still birth, 1 live birth with multiple malformations/. These data suggest that depending on the chromosome or chromosome regions involved or on other factors certain cases of reciprocal translocations may severely influence the outcome of pregnancy. Such cases are termed "malignant" reciprocal translocations.

CYTOGENETICAL INVESTIGATIONS ON THE DYNAMICS OF TUMOR CELL POPULATION.

Lydie Fadei, V.Velciu, Elvira Badea

Oncological Institute,Tissue Culture Laboratory, Bucharest, Rumania.

Cytogenetical studies during the evolution of $H_{10}Z$ Syrian hamster experimental tumor and of a human reticulosarcoma were performed.

$H_{10}Z$ tumor chromosomes were studied on 8, 17, and 33 day of tumor evolution.Human reticulosarcoma cytogenetical structure was investigated in two different periods of tumor growth by puncture of ascitical fluid.

Following results were obtained:

$H_{10}Z$ Syrian hamster tumor presents 4 cell types: A-near diploid,B-heteropleid without chromosome marker,C-heteroploid with a long submetacentric marker,D-high polyploid. During the tumor evolution takes place the gradual selection of C and D cell types. The human reticulosarcoma has different cell types with diploid and near diploid cytogenetical structure.The progressive selection of a near diploid cell type with markers accompained tumor development.

From these results it may be concluded that the studied tumors have a heterogenous structure. During their evolution takes place the gradual selection of certain cell types confering to the tumor new phenotypical peculiarities.

CHROMOSOMES IN MALIGNANT LYMPHOMAS

Tamás, Fleischmann

Institute of Genetics, Lund, Sweden and 1st Medical Department,University Medical School, Szeged, Hungary

Tumorous lymph nodes of patients suffering from malignant lymphomas were removed surgically and investigated cytogenetically. Biopsy material from 30 patients were cultured and fixed on slides. The slides were studied by normal orcein technique or by means of a fluorochrome. When needed, autoradiography was carried out, too. Results:

1. The chromosome number was usually found in diploid range, in the cases of lymphosarcomas quite consequent hyperdiploidy was observed.
2. The karyotypic changes were not unique but characteristic variations were found in B and E groups.
3. In many cases several types of marker chromosomes were recognised: long subtelocentric, long or medium-sized submedian markers and isomarkers. Some of these markers had characteristic fluorescent pattern and were displayed by computer technique as isobrightness maps and three-axis diagrams.

DOES COMPETITION BETWEEN SPERMATOZOA OCCUR ? EVIDENCE FROM EXPERIMENTAL CYTOGENETICS.

Ford, Charles, E.

Sir William Dunn School of Pathology, Oxford, England.

Backcrossed derivatives of hybrids between Mus poschiavinus and laboratory mice produce many aneuploid gametes. Observations at second meiotic metaphase and the determination of embryo karyotypes permit an efficient comparison between the expected frequency of aneuploid gametes and the observed frequency of aneuploid embryos. The results give no evidence of an influence of genome unbalance on gametic maturation or function, or on zygotic development up to about the time of implantation. They support the view that the genome is normally inactive during the haploid and early post-zygotic phases of the life cycle.

COMPARATIVE MORPHOLOGICAL AND GENETIC STUDIES IN STREAK GONAD SYNDROME AND IN CASES OF TUMOURS OF GONADAL ORIGIN

Gaál,Magda and László,János

Department of Pathology of the National Institute of Physical Education and Sport and Gynecological Departement of Postgraduate Medical School,Budapest,Hungary

The morphological structure of the streak gonad was investigated in cases of 45,X; X/XX, and X/XY streak gonad syndrome. In addition to commenting the formal genesis of the syndrome, the authors present three cases in which it has been observed that a gonadoblastoma / gonocytoma III/ can develop only from a streak gonad associated with an X/XY karyotype since it might be considered as a histologically dysgenetic testis. The cells of the tumour appear to correspond to male germ cells; female X sex chromatin has never been demonstrated in them.

PATHOLOGY OF HUMAN SEX CHROMOSOMES: AN EPIDEMIOLOGICAL SURVEY.

Giordano,A., Lavezzi,A.M., Dept.of Pathology,Univ.of Milano, Milano-Italy.

The caryological analysis of 3000 women in Milan revealed six cases of Turner syndrome. Two of them had caryotype XO,three mosaicism XX/ XO/ XXX and one mosaicism XX/ XX^{q1} /XO. In one of XO the X chromosome was paternal, as confirmed by the Xg blood group. The cases observed were carefully examined both by clinical and laboratory methods. Barr bodies were regularly present in complete Turner syndrome and observed occasionally in mosaicism and in isochromosomism. In the latter, 5% of oral mucosal cells presented Barr bodies larger than normal. Two cases of Klinefelter syndrome were studied. The blood group of the first child was Xg^+; the mother was negative. In this case the nondisjunction had possibly concerned the paternal chromosomes. The patient had deuteranomalia while his mother and a brother had normal colour vision. Another brother had deuteranomalia. Thus the mother was a heterozygote carrier of the defect,and the patient had two X chromosomes with the abnormal gene.In the other case of Klinefelter syndrome the blood group of the child and his parents was Xg^+; therefore the origin of the non-disjuncted chromosome was not detectable.In both cases high urinary gonadotropine and low testosterone levels were found.One had less than 10% spermatozoa with Y chromosome.

STAINING PATTERNS, STRUCTURE AND IDENTIFICATION OF HUMAN CHROMOSOMES.

Gropp,A., Inst.of Pathology, Lübeck-GFR.

RECENT OBSERVATIONS ON CHROMOSOMAL EVOLUTION OF MAND AND PRIMATES. De Grouchy,Jean, Hopital des Enfants-Malades,149,rue de Sèvres, Paris.

The banding technique by controlled heating denaturation was applied to the study of the chromosomes of the anthropomorphic apes: chimpanzee /Pan troglodytes/, gorilla /Gorilla gorilla/,and orang-utang /Pongo pygmaeus/. Comparisons two by two of the karyotypes of man /Homo sapiens/ and the three primates, man-chimpanzee, man-orang-utang,and chimpanzee-gorilla were made. The observations are compatible with the most generally accepted phylogenetic tree, i.e. a first separation of two branches, one giving rise to the orang-utang,the second to man and to a branch which in turn gives rise tothe chimpanzee and the gorilla. Results offer the possibility to reconstruct for each individual chromosomes a phylogenetic tree showing in which branch each rearrangement occured. Hence it becomes possible to propose a karyotype for the common ancestor of man and the anthropoid apes. Discussion bears upon the preponderant role played by centric fusions and pericentric inversions during evolution. It is estimated that on the everage it takes 5 million years for one major rearrangement to become established. It is suggested that these rearrangements which occurred in the heterozygous state became homozygous due to the high frequency of incestuous matings in primitive populations, thus allowing the progressive isolation of species. Gene mutations- which are not by themselves capable of speciation - may have occured secondarily, thus providing individualization of species.

IDENTIFICATION AND SIGNIFICANCE OF CHROMATIN WITH ENHANCED QUINACRINE BINDING CAPACITY

Kovács,Margit,Sellyei,Mihály and Vass,László

Department of Forensic Medicine Semmelweis Medical University, Pathology Department Róbert Károly Hospital, Budapest, Hungary

The presence of Y chromosome may be revealed in interphase nuclei by detection of Y chromatin. The frequency of fluorescent Y chromatin has been examined in quinacrine stained smears from several organs - brain, myocard, lung, liver, spleen, intestinal mucosa, bone marrow, striated muscle and thyroid gland - of 100 males and 100 females. In smears of male origin Y chromatin was seen in 20-93 per cent of cell nuclei. In female specimens 0-14 per cent of nuclei have shown Y chromatin like fluorescent spots. In cell nuclei of the thyroid gland both of males and females the frequency of fluorescent bodies was higher than in other organs. Double structures in male specimens were often seen. They may simulate an extra Y chromosome in males and give a false Y positive result in females. We assume that these fluorescent spots represent the organ specific heterochromatin of the thyroid gland.

THE SIGNIFICANCE OF BANDING TECHNIQUES FOR THE IDENTIFICATION OF CHROMOSOMES ABERRATIONS.

Lindsten,J., Dept.of Clin.Genet., Karolinska Sjukhuset, Stockholm-Sweden.

CHROMOSOMAL ANOMALIES IN A TRANSPLANTABLE GUINEA-PIG'S TUMOR.

Mohácsy,Judit, Vass,L., Sellyei,M., Jellinek,H.,Kádár,Anna, Haranghy,L.

2nd Department of Pathology of the Semmelweis Medical University,Budapest and Pathology Department, Róbert Károly Hospital,Budapest.

Guinea pigs' /Cavea porcellus/ normal karyotype was investigated using both quinacrine fluorescence and Giemsa-band techniques. The specimens were obtained from the bone marrow of adult animals after in vivo Colcemid treatment. The Q- and G-band patterns are mostly identical. By the same way were obtained mitoses from the transplantable Daels' sarcoma of guinea-pigs. The chromosomal number varies within a wide range. The tumorous karyotype is characterized by long metacentric marker chromosomes. New techniques enlighten the determination of normal chromosomes having taken part of the formation of the markers. The constant presence of identical marker chromosomes in cells from several transplant generations speaks rather for cellular than viral mechanism of tumor-take after transplantation.

INHERITANCE OF G/G TRANSLOCATION ACCORDING TO THEORETICAL RISKS

Papp, Zoltán; Dolhay, Balázs; Gardó, Sándor Skapinyecz, József
Human Genetics Laboratory, Department of Obstetrics and Gynecology, University Medical School, Debrecen, Hungary

The t/21q22q/ is considered to behave in a similar way to other Robertsonian translocations, and families with this type of inherited structural change can be recognized by the presence of balanced heterozygous sibs as well as affected children. If there is evidence that the translocation is of the type 21/22 because there is already a balanced sib in two families available which suggests that the risk may be less than the theoretical 1:3, but it must be remembered that these families were selected by the presence of a phenotypically normal balanced heterozygous sib.
In the family found by us the mother had four pregnancies in all four variations: a spontaneous abortion, a Down-syndrome infant, a balanced heterozygote and a healthy offspring. The heterozygote also had a child with Down-syndrome, while the healthy offspring gave birth too a healthy girl.
So in our above-mentioned case the segregation of this rearrangement was according to theoretical risks.
The pedigree and karyotype will be demonstrated.

CORRELATIONS BETWEEN SEX CHROMATIN AND ACHROMATIC GAP IN GONADAL HYSGENESIS.

Gh.Rosca, S.Rosca, Medical and Pharmaceutical Institute, Cluj, Romania.

The authors are performing cytogenetical analysis /kariotype,Barr sexual chromatin, nuclear appendix/ in 6 women patients hospitalised with different clinical forms of gonadal dysgenesis.

On the bases of their results, they follow in each case particularly the correlation between the gonosomial formula,Barr sexual chromatine and A-type nuclear appendix. The quantitative change of the nuclear sex tests is observed in patients missing an X gonosome, with a deleted X gonosome or with an X gonosome bearing an achromatic lesion..

The significance of the achromatic lesions on an X chromosome is discussed by the author.

CYTOGENETIC ANALYSIS OF THE SOME PERSONS WITH ORAL ANOMALIES /CLEFT LIP AND PALATE/.

S.Rosca and Gh.Rosca, Medical and Pharmaceutical Institute, Cluj, Romania.

The authors are performing kariological examinations in two lots of patients,exhibiting labio-maxylo-palatoskysis.
The first lot includes patients originating from families exhibiting the oral malformation only in a single "isolated" member.
The second lot is constituated by pacients originating from families in which the oral malformation has a "familial character" being apparent in at least two family members.
The kariological examinations showed normal kariograms in the first lot, while in the second one there is a significant percent of chromosomial aberrations, especially structural of the type of the group A or B chromosomes asymmetry. The ground of these asymmetries is the chromosomial deletion, followed as not by the translocation of the deleted fragments on the adjoining chromosomes.

CHROMOSOME STUDIES IN LATE ABORTIONS.

Ruzicska, Péter and Czeizel, Andrew
National Institute of Public Health, Laboratory of Human Genetics, Budapest

In a series of 188 second trimester abortuses, the chromosome complements of 97 specimens with a mean gestational age of 19.9 weeks were studied. Of these, 35 were shown to carry chromosome aberrations. The type distribution of the chromosome aberrations found was the following: 5 X monosomies, 5 autosomal monosomies, 7 autosomal trisomies, 5 double aneuploids, and 13 structural aberrations. Special features of these results distinct from those described in the literature are the high incidence of structural anomalies and the frequent occurrence of aneuploids in mosaic forms /15 of the 17 aneuploid abortuses contained besides the aberrant cell line a diploid cell line showing normal karyotype/. These pecularities may be due either to technical or population differences or most probably to differences in the mean gestational age of the abortuses studied. The results suggest that late abortions may represent a special phase of the chromosomal genetic selection taking place during intrauterine life.

PATHOGENETIC SIGNIFICANCE OF CHROMOSOMAL CHANGES REVEALED BY NEW TECHNIQUES

Sellyei M.
Dept. of Pathology, Róbert Károly Hosp. 1394 Budapest, Hungary

The biochemical basis and functional significance of bands along the chromosomes remained mostly unclear. Experiments on producing G-bands showed the importance of actual temperature of the dyeing solution, depending on the quality of a given stain. The brightness of Y-chromatin is connected with the size of fluorescent distal part of Y chromosome and its quinacrine-banding capacity. The latter may be diminished either congenitally or as a consequence of some haematological malignancies. Parallel use of various banding techniques on the same cellular divisions makes possible to elucidate the hitherto unknown origin of rearranged chromosomal set in neoplastic cells.

ABSENCE OF Y CHROMATIN IN MALIGNANT CELLS OF HUMAN MALES

Vass, L. and Sellyei, M.
Dept. of Pathology, Róbert Károly Hosp. Budapest, Hungary

The authors investigated the occurrence of fluorescent Y chromatin in the interphase nuclei of malignant cells of human male hosts. The presence of fluorescent Y chromatin i. e. Y chromosome in somatic normal cells was checked almost in every case. Out of 136 solid tumours of persons with fluorescent Y chromatin in normal cells there were 23 tumours lacking the Y chromatin /below 10%/. Detailed karyotyping was performed in one case of Y-negative adenocarcinoma using both Q-, and G-band techniques accomplished with C-bands. Fluorescent Y-chromosome was absent in all mitotic tumour cells. The high frequency of Y-negative solid tumours is contrasted to leukaemias where the absence of fluorescent Y chromosome is extremely rare.

INFLAMMATORY DISEASES OF THE LYMPH NODES

Organized by

PIRINGER-KUCHINKA, A.

Invited lecturers

CAMAIN, R., DESTOMBES, P.
HANAK, H.
KAISERLING, E., LENNERT, K., RÁCZ, P., TENNER, K.
KELLER, H. U., HESS, M. W., COTTIER, H.
KOJIMA, M., IMAI, Y.
KRAUS, B.
LAPIS, K.
LEDER, L. D.
MASSHOFF, W.
QUEISSER, W.
SCHÄFER, H.
WIDGREN, S.

AUTORADIOGRAPHIC AND STEREOLOGICAL STUDIES OF THE MIGRATION AND THE DIFFERENTIATION OF LYMPHNODE IMMUNOCOMPETENT CELLS DURING HUMORAL IMMUNIZATION

Betz, Emile-Hippolyte, Simar Léon, J
Institute of Pathology, Liège, Belgium

During the development of a humoral immunity after the single injection of an antigen, numerous immunoblasts appear early in the lymphnode germinal centers Autoradiographic studies, at the ultrastructural level, suggest that these cells originate from cortical small lymphocytes. They demonstrate also the existence of a "polarity" in the lymphnode. Indeed the immunoblasts leave the germinal centers in order to reach the medullary cords by two different ways. The majority migrates through the paracortical area whereas few of them infiltrate first the marginal sinus before they reach the medulla. Into the medullary cords they transform into plasma cells.

The stereological methods permit to characterize two important events in the differentiation of these immunocompetent cells. The first one concerns the elements of the germinal centers, during their disruption early after antigen injection. The second one,which occurs three days later, corresponds to the transformation of immunoblasts into young plasma cells in the medullary cords. Between these two developments, the immunoblasts undergo little changes as they migrate through the lymphnode.

HISTOLOGIC AND MOLECULAR ALTERATIONS IN THE CELLS OF LYMPHOID ORGANS UNDER EXPERIMENTAL PHYSICAL EFFORT.

Lucia Caluser, Babes-Bolyai Univ., Faculty of Physical Education, Dept.of Human Anatomy, Cluj, Romania.

Histologic, histoenzymatic and electronmicroscopic investigations have been carried out on thymic, splenic and lymphonodal S.R.H. cells of rats which were subjected to physical strain through swimming. One group underwent acute - stressing - effort and another a proportioned - training - effort.

Morphologic alterations were of the same lesional pattern in both groups but they differed in intensity.

A decrease in the number of lymphocytes and an increase in pyroninophil plasma cells were noted as well as numerous mast cells in thymus and lymph nodes. Enzymatic content was hardly influenced: ATP-ase, succinodehydrogenase, acid and alcaline phosphatase. Ultrastructurally, nuclear chromatine displays a marginal arrangement, endoplasmatic reticulum is swelling, mitochondrial matrix exhibit clear areas and ribosoms settle in compact clusters.

These alterations are considered as normal morphologic steps caused by a hyperactivity of the adrenal gland.

FUNGAL DISEASES OF LYMPH NODES

Camain, Robert* and Destombes, Pierre**
* U.E.R. Médecine, Laboratoire Histologie Embryologie, Nice, France
** Institut Pasteur, Laboratoire Histopathologie, Paris, France

The fungi observed inside lymph nodes appear most often as metastasis as well of cutaneous mycosis as of visceral mycosis.
Such localizations occur in a very different average according to the type of mycosis.
As a general rule mycosis due to filamentous fungi are rarely metastatic to lymph nodes ; on the contrary metastasis are frequent in yeast mycosis. The lymph nodes reactions are in some cases similar to those seen in the primary lesions, in other cases they differ from them.
These lesions are pleomorphic - non specific granulomas - specific nodules with or without caseation.
Cases of lymph node metastasis of Actinomycosis, Aspergillosis, Histoplasmosis, Blastomycosis, Cryptococcosis, Sporotrichosis, Coccidioidiomycosis are described and commented.

LYMPHADENITIS WITH MASSIVE SINUS HISTIOCYTOSIS AND LIPIDIC STORAGE (Histochemical and electronic study).

T.CAULET, A.PINTEAUX, C.HOPFNER.
Laboratoire d'Anatomie Pathologique, Faculté de Médecine. REIMS 51100 (France).

The observation of a 36 year old man who presented a relapsing massive bilateral cervical lymphadenopathy is reported. There was a prominent hyperplasia of the sinus histiocytes and also of the pulpar ones; hemocytophagia, P.A.S.positive inclusions, and lipidic storage in foamy pulpar histiocytes are striking; plasmocytes are numerous; presence of two small fibrosis surrounded necrotic areas. This condition is to compare with "sinus histiocytosis with massive lymphadenopathy" (ROSAI and DORFMAN, 1969) and with "lymphadenitis with massive hemophagocytic sinus histiocytosis" (LENNERT)* and and with the report of CANALE and SMITH, 1965. Some peculiarities are to be stressed on : hemophagocytosis is moderate, the abundant stored lipids are soudanophilic; electron microscopically, besides varied inclusions and residual bodies, histiocytes contain lipidic vacuoles,or osmiophilic inclusions, and granular proteic material; their rough granular endoplasm is often prominent; they exhibit occasionally huge nuclear pseudo-inclusions and intracytoplasmic filamentous sometimes periodic dense structures. This disease, with no demonstrable etiology, seems to exhibit metabolic trouble leading to lipidic intracellular deposits and to alterations of proteic synthesis of the lymphatic reticular cells.

K.LENNERT and al.: Virch.Arch.Abt.B.Zellpath. 10, 14-29, 1972.

THE HEMAL NODE IN THE IMMUNE RESPONSE

Folse, Dean S,
Pathology Laboratory, University of Texas Medical Branch, Galveston, Texas U. S. A.

Light and electron microscopic studies of the ruminant hemal node have confirmed it to be a distinct lymphoid structure. Vascular connections are evident but no lymphatics are present. It is composed of a fibrous capsule with some smooth muscle, a prominent subcapsular blood sinus, a network of deeper blood sinuses, lymphoid follicles with germinal centers and lymph cords. The framework of the node is made of trabeculae composed of three cell types.

The normal hemal node shows no evidence of erythropoiesis, myelopoiesis, or erythrophagocytosis. Studies of lymphocyte depleted hemal nodes suggest that they have both thymic dependent lymph cords and follicle cuff areas and bursal dependent germinal centers. Following antigenic exposure by the circulatory route using a renal allograft as a model hemal nodes become stimulated and immunologically active as judged by morphological criteria.

LYMPHADENITIS TOXOPLASMOTICA

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Toxoplasmosis of man occurs in the adults mostly as lymphadenitis. The affected lymphnodes very often are situated superficially in the neck, somewhat enlarged, mostly painless and therefore recognized only accidentally. They are moderately firm and their cut surface is inconspiciuous. Histologic characteristics are 1. small groups of epitheloid cells scattered throughout the whole organ, 2. socalled immature sinus histiocytosis, 3. hyperreactive follicles with many phagocytes and nuclear debris, and 4. inflammatory infiltrate often exceeding the capsule of the node. This histological picture is known as Lymphadenitis Piringer. Toxoplasma Gondii extremely seldom can be found, mainly in its cyst form. For confirming diagnosis patients blood should be tested by serological methods; if characteristic curves can be achieved by course controls, even the exstirpation of the lymphnode can be omitted. The results of a course study (some over more than 20 years) of about 150 patients will be presented.

LIPOID STORAGE RETICULITIS OF UNKNOWN ŒTIOLOGY IN AN ADULT EUROPEAN MALE.

Jobard,P., Benâtre,A., Lhuintre,Y., David,C. Ghaly,A.F. and Allard,J.C.

Laboratoire d'Anatomie Pathologique, Faculté de Médecine. 37000 TOURS - FRANCE.

Clinical history of chronic nasal obstruction since 9 years, in a French male, 41 years old at the first examination.

Axillary and cervical lymphadenitis and recently one left temporal cutaneous nodule appeared.

In all this localizations, the histologic pattern is the same granulomatous infiltration with numerous histiocytic foam-cells mixed with plasma cells and neutrophil polymorphonuclear leucocytes.

The œtiology of this inflammatory disease remains unknown after bacterial, viral and ultrastructural investigations.

These lesions might be compared with those of some pseudo-tumoral cervical lymphadenitis observed by French authors in black children from West-Indies and Africa.

LYMPHADENITIS CAUSED BY FACULTATIVE INTRACELLULAR PARASITIC BACTERIA, E. Kaiserling, K. Lennert, P. Rácz, and Klára Tenner

Institute of Pathology, Kiel, Germany

Among the types of lymphadenitis caused by so-called facultative intracellular bacteria L. monocytogenes infections represent a suitable experimental model, since humoral immunity plays a minor role in these infections.
The ears of 26 SPF guinea pigs were intradermally infected. Regional lymph nodes were examined light and electron microscopically. After 30 min bacteria were found in the sinuses lying both free and within monocytes and granulocytes. They rarely appeared in the retothelial cells. The reticulum cells lying near the latter and the large macrophages of the medullary sinus showed active phagocytosis. A disintegration of the lymph node parenchyma and an emigration of polymorphonuclear granulocytes and monocytes through the walls of the high endothelial venoles were observed in the interfollicular region. After 48 h the lymph nodes showed so-called bunte Pulpahyperplasie. Starting with the 3rd day the cellular infiltration became more localised: granulomas were formed, especially in the perivascular region. We could distinguish 2 types of granuloma: one containing freshly emigrated monocytes partly with intact intracytoplasmic bacteria, and one containing activated macrophages sometimes with bacterial disintegration products. A few groups of epithelioid cells could be seen from this point on. Similar changes were observed in experimental pseudotuberculosis.

LYMPH NODE STRUCTURE AND IMMUNE FUNCTIONS

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Bern, Switzerland

The lymph node structure is intimately related to immune functions. The following aspects of this relationship will be considered on the basis of combined kinetic and immunological studies: 1) Magnitude and pattern of thymic lymphocyte migration to other lymphoid tissues. 2) Kinetics of lymphocyte recirculation. 3) Sessile and mobile long lived lymphocytes 4) Morphological changes associated with cell-mediated immune responses. 5) Formation of germinal centers during primary and secondary antibody formation and their relationship to plasmacytopoiesis in the medullary cords.

GERMINAL CENTER IN IMMUNE REACTION

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Although it has been recently recognized that the germinal center cells (GC cells) participate in mechanisms of antibody production, there are many unsolved problems in details about the origin and fate of the GC cells and nature of antibody produced by them. The results obtained in this study are as follows. 1. By injection of horse-radish peroxidase (HRP) into new-born rats, the GC develops with in the primary lymphatic nodule. From the observation of their development in early stage, it has became obvious that the GC cells are originated from the desmosome-bearing reticular cells pre-existing within the primary nodules. 2. By the enzymatic antibody technique and immunofluorescence method, it has been proved that the GC cells have antibodies, especially γM, in their cytoplasma. These cells produce hemolytic plaques in the study of plaque formation according to Jerne's original method. 3. In the animals sensitized with HRP, it has been confirmed that the GC cells producing HRP antibody mostly move into the marginal sinuses of lymph nodes and flow into the peripheral circulation via the thoracic duct, though a part of them are destroyed in loco and phagocytized by macrophages.

LIGHT AND ELECTRONMICROSCOPIC CHARACTERISTICS OF ACUTE AND CHRONIC LYMPHADENOPATHY INDUCED BY DIPHENYLHYDANTOIN

Krasznai Géza, Szegedi Gyula, Lustyik György
Univ.Inst.Pathol.Debrecen.Hungary

Acute hydantoin lymphadenopathy is associated with generalized hypersensitivity reactions. Tumor-like atypical reticulum cell, histiocyte proliferation, focal haemorrhagic necrosis, thrombotic microangiopathy, plasma cells and eosinophil cells and variable destruction of the original lymph-node architecture can be seen. The result of ultrastructural analysis are: 1/ Active histiocyte and reticulum cell proliferation /H_1/ with abundant RER and mitochondria, 2/ degenerative histiocyte and reticulum cells /H_2/ with vacuoles and cisternae of RER, mitochondria, residual bodies and lipid droplets.

The chr. hydantoin lymphadenopathy is connected with long-term use of hydantoin. Lymph node biopsy reveals lymphoid depletion, nodular fibrosis, and diffuse proliferation of reticulum cells. No sign of malignant transformation is demonstrable. Fibrous tissue and H_2 type histiocyte proliferation are observed by ultrastructural study. The blastomogen effect of hydantoin cannot be confirmed.

LYMPH NODAL CHANGES IN SCLEROMA. MORPHOLOGY AND FINE STRUCTURAL PROBLEMS.

Kraus, Brigitte
Pathologisches Institut, Katharinenhospital 7 Stuttgart, BRD

The involvement of lymph nodes in scleroma is extremely rare and less known than the primary infection of the respiratory mucosa. Mainly affected are the submandibular lymph nodes. The typical morphologic changes are Mikulicz cell-like transformation of sinus cells, massive hemophagocytosis and plasmocytosis. In contrast to scleroma of the respiratory mucosa Klebsiella rhinoscleromatis has not unequivocally been demonstrated in lymph nodular lesions until now. Similar morphologic findings in cervical lymph nodes have been reported in children without any known etiologic condition. The absence of bacteria in the descripted lymph nodular changes does not exclude Klebsiella rhinoscleromatis as the active agent, for resorption of toxins or fragments might be causative. In spite of the chronic course, the disease generally is limited to the respiratory tract. This may depend on specific conditions of respiratory mucosa favourable to the pathogen. Scleroma can be considered as a special form of parasitism without destruction of host tissue, but with a typical morphologic transformation.

VIRUS INFECTION AND THE LYMPH NODES

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1st Institute of Pathology, Semmelweis Medical University, Budapest, Hungary

Exposure to cytbmegalovirus infection is a common event in the general population, disease on the other hand is rare. The natural infection at times may, however, become generalized. Widespread symptomatic CMV infections may be observed in individuals with compromised cellular defenses associated with reticulo endothelial /RE/ and other malignancies, in the fetal or neonatal period, and in the presence of certain immunologic defects. Particularly serious generalized infections have been observed also in patients with neoplastic disease following intensive treatment with corticosteroids and cytostatics as well as following immunosuppressive regimens administered to organ recipients. The isolation of cytomegalovirus from the adenoids /Rowe et al.1956/, lymph nodes /Stulberg et al.1966/ demonstrated the affinity of cytomegaloviruses for the lymphoid tissues, not much is known, however, about the virus induced alterations of lymph nodes. - Mice were infected with mouse-cytomegalovirus suspension i.p. Lymph nodes taken in various intervals following infection were studied. The alterations observed at both light and electron microscopic level will be described and compared to those seen in the lymph nodes of hamsters infected with the virus strain parainfluenza-3.

GRANULOMATOUS LYMPH NODE REACTIONS DUE TO POLYVINYL PYRROLIDONE

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Institute of Pathology, University of Kiel, Kiel, Germany

It is well known, that polyvinyl pyrrolidone can be stored in the macrophage system of lymph nodes for a long period of time. However, PVP in certain cases leads to severe granulomatous changes, which may simulate a variety of other lymph node diseases. Thus, serious misinterpretations may occur. Therefore, the clinical and morphological picture of the PVP induced granulomatous lymph node reaction will be presented together with some differential diagnostic considerations.

LYMPHANGITIS AND LYMPHADENITIS PARATUBERCULOSA

STUDY presented in a thesis to the Veterinary Faculty, University of Utrecht, by

Majeed, S.K.
Pathology department Organon - The Netherlands

The lesion of paratuberculosis or John's disease in ruminants, usually affecting the intestines appears as a "primary complex" in which the regional lymphnodes are also involved. In this study, the lymphnodes and lymphvessels from goats infected both spontaneously and experimentally with the disease were studied grossly and microscopically (light and electromicroscopy).
In the early stage of the disease, the afferent lymphvessels showed the influx of paratuberculous cells which will find its way to the subcapsular sinuses of the related lymphnode. This will be followed by the affection of the outermost zone of the cortex and later the whole cortex will be involved by the lesion. In advanced stages the influx of the paratuberculous cells in both lymphvessels and lymphnodes will be accompanied by caseation and calcification. From this finding, it was concluded that the influx of paratuberculous cells, originates from the primary lesion of the intestines and has a corticophilic affinity in the regional lymphnodes. Whereas the cells forming granulomas of noninfected paratuberculous cells in the innermost zone of the regional lymphnodes as well as in remote (non-infected peripheral) lymphnodes are formed locally. The medulla plays a little role in the pathogenesis of this disease. Changes occurring therein are described.

SYNTHESIS OF HUMAN IMMUNOGLOBULINS IN GERMINAL CENTERS AND IN PLASMA CELLS OF REACTIONAL LYMPH NODES

M. J. Mascarenhas, J. M. Forjaz de Lacerda
Institute of Pathology, Faculty of Medicine, Lisbon Portugal.

57 human lymph nodes were obtained at surgery in 46 patients with carcinoma of the breast, carcinoma of the colon, gastric carcinoma, colecistitis, and gastric and duodenal peptic ulcers. After removal of any surrounding capsular tissues, the specimens were cut into small pieces, quick frozen, and sectioned with a cryostat at -20ºC. Fluorescein labeled monospecific antibodies (prepared and comercialized by Nordic Pharmaceutica) to γ, α and μ heavy chains of the immunoglobulins and to K and λ light chains, were used in order to investigate the localization of the immunoglobulins IgG, IgA and IgM in reactional lymph nodes. The sections were examined with a Wild microscope equipped for fluorescence microscopy.
The results allow us to the following main conclusions

1 - Only one kind of immunoglobulin (most of the times IgM or IgA) is synthesized by cells in an individual germinal center.
2 - Some of the plasma cells present in surroundig lymphoid tissue of a germinal center contain one immunoglobulin, other than the immunoglobulin synthesized by cells in the germinal center.
3 - We agreed with the authors that have assumed that there are probably two lines of plasma cells in lymph nodes, only one coming from the germinal center.

THE ACUTE LYMPHADENITIS.

W.Masshoff

Dept.of Pathology,Steglitz Clinics,Free University, Berlin-DDR.

The acute lymphadenitis is a less problematic condition than the chronic one.In the lymph nodes the acute exsudative form is relatively rare and differs in features according to the ethiology and pathomechanism while the nonspecific proliferative reactions of the lymphoreticular tissue are always identical. The infection spreading along the lymphatics produces pyogenic perilymphadenitis, which may result in a purulent involvement of the lymphatic parenchyma via the capsular lymphatics. The acute lymphogenic purulent lymphadenitis is quite different from the hematogenic form seen in generalized infections or toxic conditions. The latter is characterized by focal or general circulatory damages resulting in serous, fibrinous or cellular exsudate formation and eventually in necrosis. This hyperacute form of lymphadenitis is ethiologically nonspecific. The similarly hematogenic lymphadenitis in subacute infections are in many respects fairly characteristic but still nonspecific. A typical example for this is the abscessing reticulocytic lymphadenitis. The most frequent, though not the only cause of this condition is pseudotuberculosis. A rare form of lymphadenitis of the latter type is demonstrated.

DIHYDROFOLATE REDUCTASE ACTIVITY IN NORMAL AND PHYTOHEMAGGLUTININ/PHA/STIMULATED HUMAN LYMPHOCYTES.

L.Mischiu, D.Onicescu

Dept.of Histology,Faculty of Medicine, Bucharest-Romania.

Dihydrofolate reductase activity in human lymphocytes living "in vitro" under PHA influence was estimated by an original histochemical method. During 72 hours the small lymphocytes develop an inegal enzymatic reaction /negative or week/ but the cells in PHA induced blastoid transformation show a very strong activity of dihydrofolate reductase. Only the small lymphocytes with weeak reaction are capable of blastoid transformation and self replication and during this process in small lymphocytes the enzyme activity increases.

THE KINETICS OF HUMAN LYMPH NODE CELLS STUDIED BY CYTOPHOTOMETRIC METHODS.

Queisser,W., I.Med.Klin.Fak.f.klin.Medizon, Universität Mannheim-GFR.

ELEKTRONENMIKROSKOPIE UND IMMUNELEKTRONENMIKROSKOPIE DER LYMPHADENITIS.

Schäfer,H., Abt.f.Path.d.Universität, Ulm-GFR.

LYMPH NODE LESIONS IN GASTRIC ULCER

Serrão, Daniel

Laboratório de Anatomia Patológica
PORTO, PORTUGAL

On the basis of the new concepts of the origin of lymphocytes we tried to understand the alterations observed in the lymphoid populations of peri-gastric lymph nodes and of the gastric wall itself in one-hundred consecutive cases of stomach resection by gastric ulcer.

It is assumed that beyond the lymphoid lesions dues to the interrupted continuity of the mucosal surface, we can see lesions with a immuno-pathological basis namely in lymphoid population of the gastric wall.

NEW RAPID METHOD FOR THE DEMONSTRATION OF THE LYMPHOCYTE TRANSPORMATION

L.Surján and J.Sebők
Postgraduate Medical School, Department of Pathological Anatomy, Budapest, Hungary

Intranuclear birefringence of lymphocytes stained with neutral red was measured 30 minutes after in vitro incubation with PHA or antigen against which the subject has been immunized.This early stage of the lymphocyte activation was named by RINGERTZ chromatin activation reaction.During this reaction an alteration of the structure of the DNP is demonstrated by us by means of polarization optical analysis.In our first experiment lymphocyte suspension from rat spleen was used.The birefringence of the stimulated cells increased.The mean value of this in percentage is 66,2. In our second experiment the effect of stimulation was investigated.Living cells were found even after 6-18 hours after the death of the organismus.Test for cell viability is also essential. We were able to demonstrate the reaction only if the suspension contained 10^6 living cells pro ml.So in some occasion lymphocyte transformation is demonstrable also in the routin pathological work. The advantages of our method are:1.rapidity - the result is accessible within two hours after the beginning of the stimulation; 2. economy -this method is not so expensive as the isotope technics.

MALIGNANT LYMPHOID TUMORS ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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First Dept.of Med. and Inst.Pathol.
Univ. Debrecen. Hungary.

The joint occurence of autoimmune disease and malignant lymphoproliferative tumors is not rare. We deal with those cases which occured among our patients treated for SLE in the last 20 years. We observed association of malignant lymphoproliferation /lymphogranulomatosis,lymphosarcoma,myeloma multiplex/ in 9 of our 310 SLE patients /2.9 %/

In addition we noted an intensive lymphoproliferation simulating malignant lymphoma in 4 further cases. In these cases a careful follow-up permitted the precise diagnosis.

The association of SLE and malignant lymphoid tumors reflects pathogenetic similarities between the two disease groups. Disturbance of the immunological function in patients suffering from autoimmune diseases is expressed not only in autoimmune phenomena but in the breakdown of the defense mechanism against oncogenic agents, possibly viruses. The recognition of the intensive lymphoproliferation /immuno-proliferation/ associated with SLE has a practical significance as well i.e. in forming the appropriate principles of treatment.

LYMPH NODE INVOLVEMENT IN WHIPPLE'S DISEASE

Widgren, Sven

Department of Pathology, University of Geneva, Switzerland

In Whipple's disease mesenteric lymph nodes are, as a rule, involved and show the same lesions as the gut : sheets of macrophages containing PAS positive sickleform-particles (SPC cells). Intra- and extra-cellular lipid droplets may also be found. Typical bacilliform bodies can be demonstrated by electron microscopy.

Peripheral lymph nodes are clinically apparent in about fifty percent of cases. They may show non-caseating granulomas which are often misdiagnosed as sarcoidosis or other granulomatous diseases. The PAS stain may demonstrate the typical SPC-cells, which confirm the diagnosis.

GLOMERULOPATHIES

Organized by

ENDES, P.

Invited lecturers

BÁLINT, P.
BEREGI, E., VARGA, I.
BOHLE, A.
CHURG, J.
DITSCHERLEIN, G., KETTLER, L. H., SCHNEIDER, W.
ENDES, P., SZABÓ, J., DAUDA, G.
HOEDEMAEKER, Ph. J.
MÁRK, I.
MOSTOFI, F. K., KAWAMURA, S., AIZAWA, S.
PLANK, J.
SINDJIĆ, M.
STOLARCZYK, J.

INTRARENAL HAEMODYNAMICS IN EXPERIMENTAL RENAL FAILURE.

Bálint,P., László,K., Szőcs,É., Dept.of Physiology,Semmelweis Medical University, Budapest-Hungary.

Series connected intrarenal resistances were measured in various forms of experimental acute renal failure in dogs.
1. In severe dehydration /due to ligature of the pylorus/ afferent resistance is increased,while efferent and venous resistances remain unaltered.
2. In mercury chloride-induced renal failure the early phase is characterized by enhanced afferent resistance; within some days afferent resistance is still increased and efferent resistance falls to very low values.
3. In acute tubular necrosis /caused by temporary occlusion of the renal artery/ decreased efferent resistance is compensated by the increase in afferent resistance.
In all three types of experimental acute renal failure the sharp drop in glomerular filtration rate, due to diminished glomerular capillary pressure, seems to be the decisive factor in the pathogenesis of oliguria or anuria.

STUDIES ON RENAL BIOPSY SPECIMENS BY IMMUNOFLUORESCENT AND ELECTRONMICROSCOPIC METHODS.

Beregi, Edit and Varga, István
Research Deparment of Gerontology and Second Department of Medicine, Semmelweis University Medical School Budapest, Hungary

Renal biopsy specimens of 600 patients were studied. In the present paper authors summarize their experiences obtained by the analysis of 70 re-biopsy specimens by histological, immunohistological and electronmicroscopical investigations. They compare the morphological and immunomorphological changes of the first biopsy specimens with those of the re-biopsy specimens and thus the cases could be divided into three groups:1/ healed cases, 2/ unchanged processes, where the pathologic alterations observed by the first and repeated biopsies proved to be identical, and 3/ deteriorated cases.
The relations of the presence of fibrin with glomerulonephritis and those of the clinical and morphological changes are also dealt with.

CLAFFICIATION OF THE INFLAMMATORY GLOMERULAR DISEASES.

Adalbert Bohle, Department of Pathology University of Tübingen, GFR

Based on own observations on kidney biopsies from more than 3000 Patients suffering from glomerulonephritis is attempted to classify the various types of this disease, which despite the most different terms, according to morphological observations and clinical symptoms have to be designated as entities. From more than 200 Patients serial biopsies were obtained.

In particular is pointed out:
1. Minimal proliferative, intercapillary glomerulonephritis with nephrotic syndrome (glomerulonephritis with minimal changes and nephrotic syndrome).
2. Minimal proliferative intercapillary glomerulonephritis with focal progression (the so-called focal glomerulosclerosis or focal and segmental glomerular hyalinosis) as a variety of the minimal proliferative glomerulonephritis with nephrotic syndrome.
3. Extra-, epi- or perimembranous glomerulonephritis (chronic membranous glomerulonephritis).
4. Proliferative poststreptococcal glomerulonephritis.
5. Membranoproliferative glomerulonephritis.
6. Rapidly progressive glomerulonephritis.

GLOMERULONEPHRITIS ASSOCIATED WITH HEPATITIS B ANTIGEN - IMMUNE COMPLEXES

Brzosko,W.J.,Krawczyński,K.,Nazarewicz, Teresa,Morzycka Maryla and Nowosławski,A
Department of Immunopathology and the Laboratory of Electron Microscopy, State Institute of Hygiene,Warsaw,Poland

Renal biopsy specimens from 34 children with clinical symptoms of inflammatory glomerular disease were studied by immunofluorescence,electron microscopy and histopathology.In 18 cases /52.6%/ lumpy and granular deposits of a homogenous mixture of hepatitis B antigen /HB Ag/,immunoglobulins G and M and beta 1C globulin were identified by immunofluorescence in the glomerular tufts. The membraneous localization of these complexes was ascertained by immune-electrom microscopy.They all showed strong affinity for guinea pig complement in the immunofluorescent reaction of heterologous complement fixation. Chronic membrano-proliferative glomerulonephritis was prevailing lesion in these cases.

These findings provide evidence that HB Ag - antibody immune complexes may play a primary pathogenic role in a significant number of inflammatory glomerulopathies in children subclinically infected with hepatitis type B virus.

GLOMERULOPATHIES ASSOCIATED WITH NEPHROTIC SYNDROME

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New York, N.Y.

Nephrotic syndrome can accompany practically any disease involving renal glomeruli. It is most commonly seen in the "intrinsic" renal diseases such as various glomerulonephritides, lipoid nephrosis and membranous nephropathy. Of the glomerulitides, the most important form is the membrano-proliferative or mesangio-capillary, frequently associated with low serum complement and deposition of C3 in the glomeruli. On occasion, nephrotic syndrome accompanies acute nephritis such as diffuse proliferative, extracapillary (rapidly progressive), focal (as seen in Henoch Schoenlein purpura), the hemolytic uremic syndrome. Some of the unusual forms of chronic renal disease may be associated with nephrotic syndrome among them cryoglobulin deposition, dense deposit disease of Berger and lipoprotein deposition. Lipoid nephrosis (minimal disease) is common in children but also occurs in adults. Focal sclerosis is relatively infrequent in children, but quite frequent in adults. Most of the cases of membranous nephropathy are idiopathic, but some are associated with metabolic disturbances, immune processes, renal toxins, specific infections and tumors. The intrinsic renal diseases account for probably 90-95% of nephrotic syndrome in children and 75% in adults. Of the systemic diseases, 3 (systemic lupus erythematosus, diabetes, amyloidosis) account for 20% of nephrotic syndrome in adults and all other causes for 5%.

TYPE AND STABILITY OF THE MACROMOLECULAR LINKS OF NEPHRON BASAL MEMBRANES IN EXPERIMENTAL ALCOHOLISM.

Cristea,Maria;Radu,Monica;Dusa,G.;Lakatos, G.; Onisor,I.
Institute of Medecine and Pharmacy, Histology Laboratory, Cluj-Romania.

By histological and histochemical methods the authors study the macromolecular links- of hydrogen, covalent and electrostatic type - of the nephron basal membranes and the surrounding stroma fibers in animals alcoholized for 30 days. However the PAS reaction demonstrates the thickening of basal membranes and the histological stainings a collagenisation process at the level of stroma, the research on macromolecular links-by means of NaCl in different concentrations, NaOH 1 % in alcohol of 80°, urea 8M in Sörensen buffer, PAS reaction and histological stainings for fibers-demonstrates the increase of macromolecular links lability. In alcoholism, the reduction of the links stability is previous to the degenerative lesions of nephron.

BONE MARROW CHANGES IN LATE URAEMIA

B.Dallapiccola,G.Tataranni and A.Farinelli
Medical Clinic,University of Ferrara and Department of Nephrology, Ferrara, Italy.

Significant changes have been detected in the bone marrow picture,studied on the aspirates obtained from 23 severely uraemic patients. 18 were undergoing long-term haemodyalisis. Only in 4 cases there was no evidence of hypocellularity.
The most peculiar findings observed in this group of subjects include: 1)increase in the percentage of mast-cells (18 cases); 2)increase in the percentage of eosinophils (17 cases); 3)macrocitosis and megaloblastosis,despite the intensive vitamin B_{12} and folinic acid support (13 cases); 4)increase in the percentage of reticular cells (11 cases); Gaucher cells were observed in one patient; 5)cytochemical evidence of an increase in the iron content (11 cases); 6)increase in the percentage of plasma-cells (9 cases).
These findings support the evidence of an abnormal proliferation involving different cellular series in chronic renal failure.

HISTOLOGICAL FOLLOW-UP STUDIES IN HUMAN GLOMERULONEPHRITIS (GN)

Ditscherlein,Gerhard, Kettler,Louis-Heinz, and Schneider,Wolfgang
Institute of Pathology,Humboldt-University, Berlin, German Democratic Republic

More than 300 biopsy specimens of nearly 130 cases with GN were studied histologically and partly by means of immunofluorescence techniques. In diffuse intracapillary-proliferative GN the assessment of the course of development was not difficult in most cases. In more than half of the cases the proliferation decreased or disappeared.In almost half of the cases with focal-proliferative GN repeated biopsy specimens revealed no significant improvement or deterioration; this points to the difficulty of assessment rather than to a persistence of the process. In the cases with extracapillary-proliferative GN (usually with necroses of loops) the proliferation diminished and no necroses were found in repeated biopsies. In membraneous GN a further increase was observed only in sewithin sections. - A clinically important aspect is the intervall between two renal biopsies. It depends on the type of GN and the activity of the process. This intervall may be rather short in extracapillary-proliferative GN but longer in diffuse intracapillary-proliferative GN and even longer in focal-proliferative GN. In membraneous GN a repeated biopsy only rarely seems to be necessary because of the slow progression.

MORPHOLOGICAL ASPECT IN EXPERIMENTAL POST-STREPTOCOCCAL GLOMERULONEPHRITIS.

Dobrescu,G., Stavri,N., Buiuc,D., Dept.of Pathology,Hosp.Nr.1.and Dept.of Microbiology Faculty of Medicine and Pharmacy,Iasi-Romania

The nephritogenic effect of strain Bi.Gh.of a beta-haemolitic streptococcus,group C,isolated from a lymph node biopsy,during an epidemy of sore throat associated with cervical lymphadenitis and acute glomerulonephritis was followed. Wistar rats,weighting 150g were used and sacrificedat intervals of 3 days,up to 6 weeks after the inoculation. The comparative histopathological findings were correlated with the determination of antibodies in sera and of proteinuria. Routine light microscopy revealed membrano-proliferative glomerulitis and congestion of the glomerular capillaries. Following single inoculation the alterations were progressive, persisting up to the 6th week.Beginning with the third week moderate lesions of solerosis and a tendency for capsular synechia occured. The animals inoculated with streptococcal Ag. Ab.complex in the equivalence zone showed prominent vascular lesions,while the glomerular alterations were slight,the most significant being the thickening of glomerular basement membrane. The vascular lesions appeared the most intensive when this complex was inoculated in the Ag.excess zone.

"GRANULOID"FORMATION BY RENAL TUBULAR CELLS

Endes Pongrác,Szabó Jenő,Dauda György

Univ.Inst.Pathol.Debrecen.Hungary

Kosugi - under the name granuloid and regarding it as a sign of tubular secretion - described the budding of the apical cytoplasma of the proximal tubular epithelium. Later some regarded this as a postmortal phenomenon, while Zollinger /potocytosis/ and others /blister/ emphasized its intravital origin. By ureteral ligation - as well as by other experimental procedures - granuloid is formed in great numbers after 8 hours. The original structure is restored 4 days after untying the ligature. By electronmicroscopy at first parts of the cytoplasmic ground substances protrude, later separate from the cell, floating in the tubular fluid.

In the dilated renal tubules of shock-kidneys the appearance of granuloids is very pronounced and though their number may increase even postmortally, there can be no doubt about their predominantly intravital origin. If so, they must participate in the formation of urinary casts, blocking a number of collecting tubules. Granuloid formation is an intravital, general reaction of cells in contact with hypotonic fluid environment.

EXPERIMENTAL ALLERGY AGAINST INSULIN AND DIABETIC GLOMERULOSCLEROSIS.

Fuchs,U., Lohmann,D., Menzel,Ruth, Ambrosius, H., Pohl,Annelies, Schade,J., Sörger,Karin, Timm,Gisela. - Inst.of Path. Labor.for Immunbiology and Ophthalmological Clinic of the Karl-Marx-Univ. and City Hosp. Leipzig,GDR, Inst.for Diabetes, Karlsburg,GDR.

The function of the glomerular cells is changed in diabetic glomerulosclerosis.It was investigated as to whether antibodies against insulin cause glomerular changes. Methods: guinea pigs: immunized against soluble insulin; 2 group of animals with immunsuppression /6-Mercaptopurin,Cyclophosphamid/; controls /without immunization or only Freund' Adjuvant/. - Dogs: immunized against soluble insulin; immuno-tolerant against insulin;controls.

Results: the guinea pigs showed high titer of antibodies against insulin.There was no diabetic angiopathy in the eye,skeletal muscle or rein,but a mild proliferative glomerulitis.In immunized dogs the diffuse glomerulosclerosis was heavier /with occasional nodules/ than in the controls or in insulin tolerant dogs.Diabetes mellitus could be excluded in all animals.

Conclusions: depending on species one symptom of diabetic angiopathy may be found. It is open to discussion as to whether it is right to correlate the insulin binding capacity of the antibodies in the serum with the structural consequences in tissue.

HISTOPHYSICAL INVESTIGATIONS OF ISOLATED NEPHROGENIC BASEMENT MEMBRANE.

Glöckner,R., Scheuner,G., Hutschenreiter,J. Inst.f.Gerichtl.Med.und Kriminalistik der Ernst-Moritz-Arndt-Univ., Greifswald,DDR., Anat.Inst.d.Karl-Marx-Univ., Leipzig,DDR.

Basement membranes were isolated from glomeruli and tubuli of pig kidneys by ultrasonic treatment. Lipids, which are build within the basement membrane in an orderly state, were indicated by polarisationsoptical investigations after different treatment and imbibition with media with different refractive numbers. The thickness of isolated basement membrane was measured interferenomicroscopically with the shearing method in dependence on the duration of ultrasonic treatment. A model of the submicroscopical composition of the basement membrane is explained.

ELECTROPHORETIC INVESTIGATIONS OF ISOLATED PARTS OF NEPHRON

Glöckner, Rainer and Zimprich, Peter
Institut für Gerichtliche Medizin der Ernst-Moritz-Arndt Universität Greifswald, DDR

Glomeruli and tubuli of the pig kidney were isolated by the sieving technique. The isolated parts of the nephron were homogenized with the Potter glass homogenisator as well as with ultrasonic. The soluble protein fraction was investigated in the discelectrophorese. The glomeruli and the tubuli shown a typical pattern in the discelectrophorese. The different methods of homogenization don't have an influence of the results of the discelectrophorese.

CHANGES IN THE ENZYME-ACTIVITY IN HUMAN PYELONEPHRITIC KIDNEYS.

I.Hamvas, Judit Mohácsy, F.Rényi-Vámos.
2nd Department of Pathology and Urological Clinic of the Semmelweis Medical University, Budapest.

The changes in the enzyme-activity was studied by histochemical methods in a total of 20 kidneys removed because of pyelonephritis caused mainly by stones and in biopsy specimens obtained by pole-resection. The histochemical study covered the following tests: alkaline- and acid phosphatase, non-specific esterase, succinodehydrogenase and PAS-reaction.
The activity of the above enzymes was found to decrease parallel to the grade of severity of the morphologically demonstrable damage. Increased enzyme activity was observed in the epithelial cells of the regenerating convolnted tubules. In some cases a decreased or missing enzyme activity was found in tubular epithelial cells of apparently intact morphology. This suggested the possibility that changes in enzyme activity may preceed the morphological changes.

PROLIFERATIVE GLOMERULONEPHRITIS AS SECONDARY GLOMERULAR DISEASE.

Haraszti, Antal
Department of Pathology, County Hospital, Eger, Hungary

Secondary glomerular lesions in some systemic diseases were studied.

In the period of 1961-1972 on post-mortem examination in 9 out of 17 cases of systemic diseases diffus proliferative glomerulonephritis was found. In some cases the kidneys exhibited diffus, in others focal or segmental glomerular lesions.

On the basis of the morphological examinations, the conclusion can be drawn, that the proliferative glomerulonephritis hasn't an uniform aetiology. It occurs not only as consequence of streptococcal infections but it could be a secondary disease in polyarteriitis nodosa, Goodpasture's syndrome, systemic lupus erythematosus, purpura Schönlein-Henoch, Wegener's granulomatosis etc.

Therefore it is necessary to take in consideration the possibility of systemic disease diagnosing proliferative glomerulonephritis with renal biopsy.

FAMILIAL NEPHRONOPHTHISIS WITH DOMINANT INHERITANCE.

L.H.L.Hjelt, Central Laboratory of Pathology, University of Helsinki, Helsinki - Finland.

Histopathological and electronmicroscopical findings in kidney biopsies are described.

PROTEINURIA AND GLOMERULOPATHY IN CLINICAL AND EXPERIMENTAL PATHOLOGY.

Hoedemaeker, Ph. J.
Department of Pathology, University of Groningen. Groningen, The Netherlands.

In rats a spontaneous glomerulopathy can be observed which appears to be related to increasing age. The etiology of this glomerulopathy which presents itself as a local focal glomerulosclerosis, is still obscure.
In experiments performed on a strain of Wistar rats we found that this glomerulosclerosis is related to the height of the spontaneous proteinuria occurring in these rats.
In human pathology also a form of local focal glomerulosclerosis is known, which was first described by Rich. This form of glomerulosclerosis which in many aspects resembles the glomerulosclerosis found in rats, always is associated with proteinuria.
In order to try out the hypothesis that in human pathology there also exists a relationship between proteinuria and local focal glomerulosclerosis, the clinical history of a number of patients showing this form of glomerulopathy was studied.
This study lent support to the theory that in human pathology proteinuria at least to a certain extend, may cause or influence the local focal glomerulosclerosis found in renal biopsies.

EFFECT OF SEX HORMONES ON THE DEVELOPMENT OF RENAL TUBULAR NECROSIS IN MICE TREATED WITH CHLOROFORM

S.Kruś, Z.Zaleska-Rutczyńska, A.Naciążek - Wieniawska
Department of Pathological Anatomy, Department of Histology and Embryology, Institute of Biostructure, Medical Academy in Warsaw, Institute of Drug Research in Warsaw

Chloroform causes the necrosis of renal tubular epithelium in male mice, and fails to exert such effect in females. Castration protects males of the strain C3H/He which otherwise inevitable die because of tubular necrosis and calcification. Castration of females does not create conditions for the appearance of chloroform-induced necrosis, and the administration of estradiol to males does not prevent the latter. Some females treated with chloroform and testosteron develop tubular necrosis.

ALTERATIONS IN THE MORPHOLOGY OF GLOMERULONEPHRITIS DURING CHRONIC HAEMODIALYSIS

Mágori, Anikó and Ormos, Jenő
Department of Pathology, University of Medicine, Szeged, Hungary

The renal lesions observed after chronic haemodialysis did not differ essentially from those observed in cases treated conservatively. There was, however, a difference in the severity of changes. The obsolescence of glomeruli became more widespread. The difference between tubular atrophy and hypertrophy was more conspicuous. The most striking feature was the extremely severe mucoid intimal thickening of the arteries, especially in those cases, which had been bilaterally nephrectomized because of hypertension.

IMMUNOLOGIC TOLERANCE, IMMUNITY AND EXPERIMENTAL NEPHRITIS.

Márk, I. 2nd Department of Pathology of the Semmelweis Medical University, Budapest.

The possible interrelationships of immuntolerance, immunity and experimental nephritis were studied by clinical and morphological methods using the Masugi model, in duck-rabbit combination. Newborn rabbits given a single large dose of nephrotoxic duck serum in their early post-natal life failed to develop nephritis after the injection of a second, low but still effective dose of the same serum at any time within the first five months of age. These animals were, however, shown to have antibodies produced to the second dose of serum. Both the development of nephrotoxic serum nephritis and the production of antibodies were inhibited in animals adequately treated with the immunosupressive drug, IMURAN.

NEPHROTOXIC SERUM NEPHRITIS AND THE ARTHUS PHENOMENON.

Molnár, Erika; Márk, I.; Halmai, Zsuzsa; Kerényi, T.; Kuruncz, S.; Gerő, G.

2nd Department of Pathology of the Semmelweis Medical University, Budapest.

The possible relation between the nephrotoxic serum nephritis and the active, local Arthus phenomenon was studied by immunological and morphological methods using the Masugi model in duck-rabbit combination. Arthus phenomenon could be produced with bovine serum albumin, cock-serum and also with the nephrotoxic duck serum in rabbits 2 to 5 months of age having been given a single dose of nephrotoxic duck serum in their early postnatal life. Authors draw attention to the fact, that while the nephrotoxic serum failed to produce nephritis it did produce Arthus phenomenon in the same group of rabbits.

MORPHOGENESIS OF THE GLOMERULAR OBSOLESCENCE : AN ELECTRON MICROSCOPICAL INVESTIGATION.

Monga Guido, Canese Maria G., Mazzucco Gianna, and Mollo Franco,
Centro di Microscopia Elettronica della Facoltà di Medicina, and Istituto di Anatomia e Istologia Patologica, Torino, Italy.

Forty human renal biopsies, out a file of 160, showed a total of 59 glomeruli useful for an electron microscopical study on the development of glomerular obsolescence. In the present material obsolescence occurred through different processes, as a consequence of :

I) centripetal compression of the glomerular tuft, by exudation, crescents, or intracapsular fibrosis (such as in proliferative glomerulonephritides, or in hypertensive changes);

II) enlargement of the mesangium with cellular hyperplasia and / or deposition of pathological material into the matrix (such as in diabetes, amyloidosis, and different chronic, membranoproliferative and lobular glomerulopathies);

III) mixed extra- and intrafloccular changes.

The most characteristic features of type I obsolescent glomeruli are a) atrophic and degenerative changes of the podocytes with "naked" basement membranes, b) entrapping of visceral epithelial cells among basement membranes of the collapsed glomerulus, and c) neoformed capillary channels penetrating from the periglomerular connective tissue across the Bowman's capsule and the intracapsular fibrous tissue. Type II obsolescent glomeruli show pathological mesangial depositions and mesangial cell hyperplasia (followed by degenerative changes) with centrolobular and/or circumferential interposition around the primitive capillaries. The latter are moved apart from the urinary space, "immured" in the sclerotic matrix and undergo atrophy. In all obsolescent glomeruli the epithelial and endothelial cells are distinguishable from the mesangial cells because of the production of peculiar basal lamina-like material.

EXPERIMENTAL PRODUCTION OF NON-NEPHROTOXIC TUBULAR NECROSIS IN THE MONKEY

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Armed Forces Institute of Pathology
Washington, D. C. 20306, U.S.A.

We wish to report the induction of acute renal failure and acute tubular necrosis in monkeys by a simple experimental procedure. Water and food were withheld for 16 hours. Animals were bled 20-25% of their estimated total blood volume; after 2 hours they were given type A human blood in the amount of 80% of the removed blood. Withholding water and food for 24 hours gave more consistent results. The animals developed hematuria, oliguria and anuria; elevation of BUN and fall of urea clearance. Structurally, focal epithelial necrosis was seen in the proximal convoluted tubules beginning at 30 minutes and reaching its maximum by the third day. The distal convoluted tubules also showed changes but these appeared to be related to the presence of casts.

QUANTITATIVE AND QUALITATIVE GLOMERULAR CHANGES IN PRIMARY AND METASTATIC RENAL CARCINOMAS.

V.V.Papilian, D.Muresanu, L.Olteanu
Histological Department, Medical and Pharmaceutical Institute, Cluj, Romania.

The quantitative and qualitative glomerular changes were studied in 30 necropsied cases /15 primary carcinomas of hypernefroma and clear cell carcinoma type and 15 metastases of bronchopulmonary undifferentiated carcinoma/.

No quantitative changes of the glomeruli in both co tical and juxtamedullar mon invaded areas were observed. The qualitative glomerular changes were represented by focal glomerulitis, as well as by extracapillary subacute glomerulonephritis.

The possible mechanisms of these glomerular changes are discussed.

THE DEVELOPMENT OF THE RENAL CORPUSCLE.

P l a n k , Julius
Department of Pathology, Komensky's University, Martin, ČSSR.

The renal corpuscle developes from the mesonephric tubule which creates a double walled cup-the Bowman's capsule. In this breaks a knot of capillaries-the glomerulus. In the development are three stages. In the first is only a lunoid vesicle with a few capillaries in the concave part of this. In the second is a spherical encapsulated tuft of capillaries and in the capsule is a columnar radial arranged epithelium. In the third are mature renal corpuscles. By the time of birth we see all the three stages. In the postnatal time there are created additional corpuscles. The first stage of developing corpuscles is located under the surface of the kidneys and in the deeper part of the cortex are more matured corpuscles. Because the function of the kidneys is from the first postnatal minutes life-important we evaluated the three stages in kidneys of newborns. We have found that in immature newborns the relation between immature and mature corpuscles is 3:1, in mature newborns 1,5:1, but after 10 days of postnatal life the relation in immature newborns is 1,5:1 and in mature ones 1:10. In the postnatal life there is a very quick maturation of corpuscles. Such evaluation declarates whether the stage of maturation of the kidneys correspond to the maturation of the newborn or not.

GLOMERULAR LESIONS IN ADULT RENAL THROMBOTIC MICROANGIOPATHY

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Laboratoires d'Anatomie Pathologique et de Microscopie Electronique, U.E.R. Médicales, Université de Nancy I, France

The haemolytic uraemic syndrome (H.U.S.) is seldom encountered in adults : in 36 cases reported in the medical literature, 32 were observed in women, 45 % in the post-partum.

The case of a 36 year-old woman is described. She presented with post-partum acute renal failure associated to haemolytic anemia of the microangiopathic type with thrombopenia.

A renal biopsy performed on the 20th day evidences a fibrinoid necrosis of some afferent arteriolae, and glomerular capillary loops slightly thickened with a few areas of focal necrosis. A second biopsy ten days later shows more marked lesions :

- arteriolar, complicated with fibrinoid thrombi
- glomerular, with thrombosis and necrosis of certain loops, ectasia in other loops, containing fibrinoid material.

The capillary walls are thickened with pseudo-duplication of the basal membrane. In electronmicroscopy, the capillary lumen is filled with material rich in cellular fragments (mostly platelets). Moreover, a deposit can be seen between the basal membrane and endothelium, sometimes containing altered platelets. However, lesions of thrombotic microangiopathy are note observed at the level of hepatic sinusoids (biopsy).

This case does not account for disseminated intravascular coagulation, but rather thrombotic microangiopathy, in which the kidney should be the mainly injured organ.

ULTRASTRUCTURAL GLOMERULAR LESIONS IN CASES WITH MINIMAL INVOLVEMENT BY SYSTEMIC LUPUS ERYTHEMATOSUS /SLE/

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Department of Pathological Anatomy
Institute of Biostructure, Medical Academy
Poznań, Poland

The aim of the current study was to examine the ultrastructural lesions of a selected group of 20 renal biopsies having minimal or mild lesions by light microscopy. Under the electron microscope all biopsies were abnormal The lesions concerned glomeruli, tubuli and interstitial tissue. The most significant were the glomerular changes, especially those of basal membranes and mesangium. The membranous lesions observed in our cases were characteristic rather for membranous glomerulonephritis. However the thickening of basal membranes was focally more marked and intramembranous dense deposits were more extensive than in membranous glomerulonephritis. The number of mesangial cells and the content of matrix were increased. Few delicate dense deposits were seen in the mesangial matrix. The endothelial cells showed swelling of the cytoplasm with occasional obliteration of the capillary lumen by the cell bodies. In one case only microtubular virus-like structures in the endothelial cytoplasm were observed.

The observed changes are not significant for SLE. Ultrastrutural studies carried out in this stage of disease however may be useful in diagnosis of lupus nephritis.

THE IMPORTANCE OF INTRAVASCULAR COAGULATION IN GLOMERULAR PATHOLOGY

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Department of Pathology, Catholic University Nijmegen, The Netherlands

More than 50 years ago glomerular microthrombosis was described in detail. Only recently the therapy of intravascular coagulation was introduced in the prevention and management of many glomerular diseases.

The intraglomerular substance may present a wide variety, e.g. aggregates of platelets, fibrin, immune complexes and probably also other plasmatic substances. Not only the composition of these substances but also their interaction is of importance for the further development of the lesion. Furthermore one must distinguish between the autochthonous formation of the coagula and the development elsewhere in the circulation followed by the embolic deposition in the glomerular capillaries.

A more efficient treatment of renal failure results in a longer survival after a period of intravascular coagulation. In these cases organisation of the intracapillary depositions can be observed. Not only in cases of focal glomerulopathy but also in more diffuse lesions such a histogenesis must be considered. In support of these views the glomerular pathology of the following morbid conditions are illustrated and discussed: 1 Renal failure in shock, 2 syndromes of intravascular coagulation, 3 Bacterial endocarditis, 4 Collagen diseases, 5 Glomerulonephritis, 6 Toxemia of pregnancy, 7 Renal transplantation.

ELECTRON MICROSCOPICAL INVESTIGATION ON INTRAVASCULAR COAGULATION IN THE HUMAN RENAL GLOMERULUS

Schuurmans Stekhoven J.H. and U.J.G.M. van Haelst
Institute of Pathology, Laboratory of Electron Microscopy, University of Nijmegen, The Netherlands.

Out of a total of 230 renal biopsies, studied by electron microscopy, intravascular coagulation is found in 49 biopsies (21%) performed in 42 patients. Of these 49 biopsies 22 were taken from 17 patients with a transplanted kidney, and 27 from 25 patients with various glomerular diseases.

In 31 out of the 49 biopsies aggregates of fibrils without distinct cross striation, are found mostly solitary and in varying numbers in the capillary lumina of the glomerulus. In the remaining number of the cases, the capillary lumen is filled partly or completely with material which shows a great diversity of its ultrastructure. Desintegrating erythrocytes, macrophages, remnants of endothelial cells and sporadically some thrombocytes can be found in this material. In these cases, the normal endothelial lining of the basement membrane has partly or completely disappeared. Besides, pictures will be shown which suggest re-endothelialisation of the lumen.

By comparative study of sequential biopsies it will be tried to give an answer to the question if and to which extent the morphological aspects of intravascular coagulation changes with time.

THE GLOMERULOPATHY OF BACTERIAL ENDOCARDITIS

Silva Duarte
Institute of Pathology, Faculty of Medicine, Lisbon - Portugal

The kidneys of seven cases with bacterial endocarditis were studied by optic microscopy and immunofluorescence.

The glomerular lesions were observed in five cases and having not a constant morphological pattern. Anyway there was a very good correlation between the lesions and the deposits of immunoglobulines and complement. In our opinion the glomerular lesions are the result of injury by immune complexes. The different aspects we have observed were nothing but the evolutive aspects of this glomerulopathy, particularly in immunohistology.

THE PATHOLOGICAL CHANGES OF KIDNEYS IN ENDEMIC NEPHROPATHY IN SERBIA

Miodrag Sindjić
Institute of pathology, Medical faculty, University in Belgrade, Yugoslavie

Endemic nephropathy is a chronic, oligosymptomatic, progressive renal disease that occurrs endemically in some balcanic states and finly brings to death most frequently from uraemia. Morphologically, early stages of the disease are not known. The autoptic material presents late stages of development of the disease. During 16 years there have been 33 autopsies of the cases of EN. Kidneys were bilaterally strongly reduced in size/both weighed 90 gm. on the average/, with smooth, finely nodular surface. Histologically, the most impressive changes were in cortex in sense of predominantly acellular interstitial fibrosis of different intensity, with glomerular and tubular atrophy, especially of lower segment. Vessels were not charactristic. It is thought that is type of chronic interstitial nephritis, probably of toxic origin, not described by now.

ULTRASTRUCTURE OF THE GLOMERULI IN HEREDITARY NEPHROPATHY (Alport's syndrome).

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Hlava I. Institute of Pathology, Faculty of Medicine, Charles University, Prague, Czechoslovákia

Renal needle biopsy was performed in 3 females (age 41, 34, 12) from a family with high incidence of hereditary disease, which manifested itself by chronic renal insufficiency and deafness in males and by hematuria in females. No characteristic changes were observed on light microscopy. Electron microscopy showed in a few loops of the glomerular capillary tuft local heavy disarrangement of the glomerular basement membrane, which was composed of an irregular network of loose strands and was markedly thickened and thinned. Complete interruptions of the continuity of the basement membrane were rarely noted in the mesangial position. The findings were very similar to those described recently by Hinglais et al. and were quite characteristic. An analogous picture was observed in a renal biopsy of a boy (age 12) from another family, where a subsequent investigation revealed a high incidence of renal disease.

RENAL BIOPSY AS A KEY TO IMMUNOSUPPRESSIVE TREATMENT IN GLOMERULONEPHRITIS

Stolarczyk Julian

Institute of Pathology,
Department of Pathophysiology,
Gdańsk, Poland

Based on 1200 renal biopsies the morphological criteria for the evaluation of the activity and degree of glomerular involvement was established.

Fourthy cases of glomerulonephritis in children was observed in the years 1967-72 and the correlations between morphological involvement, some clinical parameters and influance of cyclophosphamid treatment were investigated.

The best results of treatment were achived in cases with mild mesangial and endocapillary proliferative glomerulonephritis, but some cases with membrano proliferative glomerulonephritis and proliferative glomerulonephritis with crescents also remarkably improved.

It was impossible to find a close correlation between the morphological type, degree of glomerular involvement and the effects of cyclophosphamid therapy.

ULTRASTRUCTURE OF GLOMERULI DISSECTED FROM HUMAN RENAL BIOPSIES

Christian Svalander, Department of Pathology University of Gothenburg, Sweden

In order to enhance the morphological information from renal biopsies and reduce the histotechnical work needed, a method for processing dissected glomeruli for electron microscopy was developed.

With fine pointed tweezers in a dissecting microscope at 100 x magnification, glomeruli from small pieces of OsO_4 treated tissue were collected, transferred to gelatin capsules, dehydrated in ethylalcohol and infiltrated with Epon. A small pellet of densely packed glomeruli was obtained by slow speed centrifugation. The material was polymerized, sectioned and contrasted with standard methods. Small pieces of whole tissue from the original biopsies were processed in the usual way for comparison.

With this technique ultrathin sections containing 6 - 10 glomerular profiles within a small area can be obtained. Careful preparation minimizes mechanical artifacts. The glomerular basement membrane seems to resist the treatment satisfactorily. The ultrastructure as compared with sections from whole blocks of tissue is not inferior. The main advantage of this method is that several glomeruli from one biopsy are available for simultaneous analysis with a minimum of blocks and sectioning needed.

IMMUNCOMPLEX GLOMERULONEPHRITIS ASSOCIATED WITH HODGKIN'S DISEASE

Szabó Jenő, Szabó Tibor, Lustyik György

Univ.Inst.Pathol.Debrecen.Hungary

In a 40 year old male patient suffering from Hodgkin's disease, the symptoms of nephrosis-syndrome developed simultaneously with the deterioration of his condition. After irradiation of the enlarged lymphnodes the nephrotic-syndrome diminished. At the beginning of his last remission needle-biopsy was performed.

Histological changes corresponded to a prolonged membranous glomerulonephritis. By immunofluorescence a mainly linear-type binding of anti-IgG could be observed. Electronmicroscopically an unevenly thickened glomerular basement membrane was to be seen with granular and linear deposits and with fusion of the foot processes.

In the 5th year of his illness the patient died. Histological examination revealed the picture of a membranous glomerulonephritis, similar to the one seen in the bioptic material.

According to authors the development of the immuncomplex glomerulonephritis might be explained either by the lymphogranulomatous tissue proliferation, or by the antigen/antibody reaction induced by a virus infection as the supposed etiological factor.

MORPHOLOGICAL DATA ON THE ALTERED PERMEABILITY IN GLOMERULAR RENAL DISEASES.

Szepesházi, K., Lapis, K., Miltényi, M., Visy, M., Beregi, Edit, Szporny, Gy.

1st Institute of pathology, 2nd Department of Pediatrics, Geronological Research Group, Semmelweis Medical University, Budapest and County Hospital, Miskolc, Hungary.

Under normal conditions the glomerular filtrate passes mostly through the filtration spaces between the foot processes of the epithelial cells. In renal diseases associated with proteinuria both number and area of the filtration gaps decrease for the "fusion" of the foot processes, and the materials crossing the basement membrane may principally pass through the cytoplasm of the epithelial cells.

Authors studied the changes in the pinocytotic activity of the epithelial cells in human kidney biopsy specimens. It is suggested that in diseases producing the "fusion" of foot processes the accumulation of dense substances along the basement membrane in the cytoplasm of epithelial cells may also be a permeability regulating factor. In such cases, namely, the pinocytotic vacuoles are demonstrable only in those regions of the cytoplasm where no increase in density occurs. Actually no vacuoles were found in the area of accumulation of the dense material.

EXPERIMENTAL GLOMERULOPATHY DUE TO RARE EARTH METAL COMPLEXES

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Dept. of Forensic Medicine, Semmelweis Univ. Medical School
Budapest, Hungary

Intravenously administered organic compounds of rare earth metals form complexes with various se-proteins. These complexes are taken up in the RES-cells, but can be demonstrated also in the glomeruli. The glomerular localisation and the whole morphology resembles the ag-ab nephropathies, especially lupus nephritis, i.e. no specific localisation is demonstrable.

Combined administration of organic compounds of rare earth metals and other colloidal substances results in generalised Shwartzman-Sanarelli phenomenon.

LES GLOMÉRULOPATHIES CONGÉNITALES.

Georgette Teratuta Cordun, Gh.Scripcaru
L'Institt.Medicine et L'Morph.Nr.2.
Iassy - Roumanie

En étudiant quelques cas de glomérulopathies congénitales, avec des lésions a divers stades d'évulution /tuméfaction de la membrane basale, prolifération extracapillaire, épaississement en croissant de la membrane capsullaire et hyalinisation glomérulaire/ les auteurs concluent que les lésions sont soumises a un déterminisme pathogénique autoentretenu par diverses épines irritatives de l'organisme maternel qui traversent la barriere du placenta en lésant avec prédilection l'élement glomérulaire rénal foetal.

Les auteurs passent en revue les possibilités dans les quelles le passage transvillositaire d'une serie des facteurs maternels normaux ou pathologiques, peuvent influencer l'évulution du foetus.

COMPARISON OF GLOMERULAR CHANGES OF PATIENTS TREATED WITH ORAL ANTIDIABETICS AND THOSE WITH INSULIN THERAPY.

/ A preliminary report /

Temes,Judit - Simonyi,Klara - Lambrecht,M.
Department Hospital "Korányi",Budapest,Hungary.

As a part of a continual study on vascular changes of orally medicated diabetics,beginning the 1.6.72 so far as 28.2.73 kidneys of 61 necropsies were examinated.43 of them were medicated 1-15 years with oral antidiabetics/Group I/ 18 received 1-9 years Insulin/Group II/.The average age for Group I was 72 years and 71 years for Group II.Not included were patients with a therapy changed least than one year.Omitted were kidneys with macroscopical signs of severe pyelonephritic changes and those showing advanced vascular damage/i.e.unspecific hyalinosis of more than 25 p.c. of glomerula on repeated microscopic examination/.Formaldehyd-fixed sections,measuring 2.5x2 cm in average,were treated with H.E., PAS,Azan,Gomori's reticulum silver stain and the Kimmelstiel-Wilson stainig methode.To avoid mistakes coming from discutably specific changes,only classic signs of intercapillary nodular glomerulosclerosis /INGS/ as described by Kimmelstiel and Wilson,were counted.INGS were found 6 times in Group I and one times in Group II.

Considering available clinical data,we may conclude the greater incidence of INGS in patients treated with oral antidiabetics to be also a consequence of long-lasting inadequate and uncontrolled medication as the literature proved to be it in insufficient Insulin therapy.

HORMONE-INDUCED CHANGES OF ENDOMETRIUM

Organized by

DALLENBACH-HELLWEG, G.

Invited lecturers

deBRUX, J., SCHACHTER, A.
DALLENBACH, F.
DALLENBACH-HELLWEG, G.
FETTIG, O.
GOMPEL, G.
HOLZNER, J. H.
NORDQUIST, S.
SCHMIDT-MATTHIESEN, H.
STOLL, P.
TOTH, F.- KERÉNYI, T.

MORPHOLOGIC CHANGES IN THE ANOVULATION STERILE ENDOMETRIUM.

Alessandrescu, Dan; Bedivan, Maria and Constantinescu, Aurel.

The clinic of Obstetrics and Gynecology POLIZU, The Laboratory of pathologic anatomy. Bucharest, Romania.

- The morphological aspects of the endometrium obtained by biopsy curretage have been studied in a group of 5o women with anovulation sterility. The diagnosis of anovular cycles has been ascertained through the basal temperature curve, the aspect of cervical slime, vaginal cytohormonal examinations and hormonal measurements.
- Comparing the histological pictures (the hypoplasic endometrium, the proliferative endometrium, the hyperplastic endometrium with nonsecretory glandular hyperplasia, the endometrium with incipient or mild secretion and unequally developed endometrium), with the data obtained by hormonal measurements (estrogen, pregnandiol, 17-ketosteroids) no similarity could be ascertained. Although in a large number of the cases the histological picture was the result of estrogen activity the data yielded by measurements were below the normal.

CHANGES IN THE ENZYME ACTIVITY OF HUMAN ENDOMETRIAL TISSUE;

Bagdány S.dr, Szabó G.
Budapest, Hungary
Postgraduate Medical School. Dept. of Obst. and Gynec.

There are closed relations between steroid synthesis and enzymes activity. Estrogens increase the ensymes activity of human endometrium; but their activity decreased in the secretory-phase-i.e.progetogen-.

We studied the endometrial acid, and alcalin phosphatase, and lactase dehydrogenase enzymes activity of the endometrium. It was foundthere is a significant difference between the above mentioned phases.

The alcaline phosphatase enzymes activity proved to be more sensitive than those of the others.

The estrogens increase the protein syntheses. Maybe our findings are the result of this phenomenon.

On the base of our observations it is possible, these data will approach the more exact clinical diagnosis.

PROGESTERONE HIGH LEVELS ACTION ON DYSPLASIAS AND CARCINOMAS IN SITU OF THE ENDOMETRIUM.

J.De Brux and A.Schachter
Paris - France

The authors report their experience on 12 adenomatous dysplasias and carcinomas in situ of the endometrium treated by I.M. injection high levels of medroxyprogesterone, in young women from 25 to 39 years old.

The therapeutic tactic:

After complete curettage of the endometrium 400 mg of progestative were injected during 4 months.

After this period a new curettage was performed, and the patient was submitted to a progesterone oral contraception.

The second curettage has shown, a massive decidual transformation of the dysplasia or cancer in situ with in the bottom persistance of very few endometrial glands with cytological sign of regression.

The results are so summarized: amenorrhea during 18 months followed by - hypotrophic endometrium - normal endometrium by biphasic cycle - 3 pregnancies and delivery at term - 2 hysterectomies for other causes do not show any endometrial lesions.

The authors try to classify the atypical endometrium which benefit of this hormonal therapy.

PROGESTERONE EFFECTS ON NUCLEIC ACIDS AND SOME NUCLEASES ACTIVITIES IN ENDOMETRIUM.

Casian-Joandrea Claudia and Prundeanu Cornelia.

Department of Histology, Faculty of Medicine Bucharest - Romania.

In progesterone-administred rat endometrium the variations of nucleic acids were cytophotometrically estimated and the variations of some nucleases (acid and alcaline DN-ases, acid, alcaline and latent RN-ases) were studied by means of an original histochemical demonstration.

Progesterone gradually induced marked variations of DNA and RNA values in nuclei of the epithelial and connective tissue cells. The nucleases activities was also modified by progesterone action, predominantly in chorionic cells.

THE ACTION OF SEX HORMONES ALONE OR COMBINED ON THE ENDOMETRIUM OF ANIMALS AND IN TISSUE CULTURE.

Dallenbach,F., Inst.of Exp.Path., Heidelberg GFR.

The action of the sex-hormones either alone or combined, on the various components of the endometrium of various species of animals is discussed and demonstrated with the aid of numerous microphotographs.

Diagrams and sketches are used to explain how target cells take up estrogen, progesterone or gonadotropin and relaxin, and how these hormones act on the cell nucleus to initiate either cellular growth, proliferation or differentiation.

The morphological changes discussed are then correlated with the latest results of biochemical and radioautographic studies.The conclusions drawn are compared with those obtained in the culture of endometrial tissue in vitro before dedifferentiation has occured.

DAS ENDOMETRIUM BEI NORMALER OVARIALFUNKTION

Dallenbach-Hellweg,G.,Frauenklinik d.Univ., Mannheim-GFR.

Im normalen Menstruationszyklus erfolgt eine Proliferation des Endometriums.Mitosen in Drüsenepithelien und Stromazellen sind zahlreich.36 Stunden nach der Ovulation werden lichtoptisch die ersten Progesteroneinwirkungen fassbar.Während der ersten Woche nach der Ovulation stehen die Veränderungen am Drüsenepithel,während der zweiten Woche die der Stromazellen im Vordergrund.Sie ermöglichen eine Tagesdiagnostik während der Sekretionsphase des Zyklus.Die wichtigsten Kriterien sind:basale Vakuolen und Abrundung der Kerne der Drüsenzellen am zweiten,dritten und vierten Tag post ovulationem,Rückkehr der Kerne zur Zellbasis am 5.und 6.Tag p.o.,zunehmende Sekretion in das Drüsenlumen am 5.,6.und 7.Tag p.o.,zunehmende Differenzierung der Stromazellen zu kleinen endometrialen Körnchenzellen und grossen prädeziduale Zellen vom 8.Tag p.o.an,prädeziduale Umwandlung in Umgebung der Spiralarterien ab 9. Tag p.o.,unter dem Oberflächenepithel ab 10. Tag p.o.,der gesamten Kompakta des Endometrium ab 11.Tag p.o.,sägeblattförmiger Kollaps der Drüsen unter Höhenabnahme ab 12.Tag p.o., beginnende Dissoziation der Stromazellen ab 13.Tag p.o. Der Kollaps der Schleimhaut wird durch Oestrogenabfall am Zyklusende mit Wasserverlust ausgelöst,die Dissoziation des Stromas durch Relaxinausschüttung infolge Abfalls des Progesteronspiegels.Beide Vorgänge führen zur menstruellen Abstossung der Schleimhaut.

HISTOLOGISCHE VERANDERUNGEN AM MENSCHLICHEN ENDOMETRIUM UNTER REINER OESTROGENZUFUHR, REINER GESTAGENZUFUHR UND ZUFUHR KOMBINIERTER HORMONE.

Dallenbach-Hellweg,G., Frauenklinik d.Universität, Mannheim-GFR.

Reine Oestrogene führen bei kontinuierlicher Einwirkung exogener kleiner bis mittlerer Dosen zu ungehemmtem Wachstum /gland. cystische Hyperplasie - adenomatöse Hyperplasie, ggf. Carcinom/; bei Einwirkung toxisch hoher Dosen: zur Zerstörung, bzw. funktionellen Auslöschung der Rezeptoren mit Atrophie des Endometrium. Reine Gestagene führen bei kontinuierlicher exogener Einwirkung zunächst zur starren Sekretion und schliesslich zur irreversiblen Atrophie des Endometrium. Dabei ist weniger die Dosis als in erster Linie di Dauer der Verabreichung massgebend für das Ausmass der Veränderung. Beide Hormone kombiniert führen je nach Überwiegen der einen oder der anderen Komponente zu den entsprechenden isolierten Hormonwirkungen.

AUTORADIOGRAPHIC STUDIES ON HUMAN ENDOMETRIUM UNDER EXOGENIC HORMONAL INFLUENCE.

Fettig,O., St.Vicentius-Krankenhaus, Karlsruhe-GFR.

The DNA synthesis in human endometrial tissue specimens was studied by deeping autoradiography after incubation in H^3-thymidine.Depending on the time of ovulation the DNA synthesis in the glandular and surface epithelia increased in the first and decreased in the second half of the cycle. The RNA and protein synthesis of the same tissue elements appeared to be quite constant and independent of the cycle. In the premenstruum the DNA synthesis increased conspicuously in the perithel and adventitia cells of the stroma. In cases of glandular-cystic hyperplasia the H^3 labeling was marked in the glandular-, and moderate in the cystic areas with little proliferation of the stroma. In Primosiston--induced mucosa there was an intensive DNA synthesis in the stroma while none was demonstrable in the glands. A 15 months' period of daily treatment with 0.075 mg Mestranol and 2.5 mg Lynestrenol resulted in reduced or nuchanged proliferation of glandular and surface epithelium and in a moderately increased proliferation in the stroma throughout the cycle. Nevertheless as compared to the controls no significant change in DNA synthesis could be detected in the endometrium following exogenic hormone administration.

ELECTRON MICROSCOPY STUDY OF HORMON-INDUCED CHANGES OF ENDOMETRIUM.
Gompel,G., Inst.Jules Bordet, Bruxelles-Belgium.

THE REGENERATION OF NORMAL AND ALTERED ENDOMETRIUM AFTER CURETTAGE
Gyergyay,Francis P., Gyergyay-Malatinszky, Éva S. and Rónai E. Magda
Institute of Medicine and Pharmacy, Dept.of Pathology, Tîrgu-Mureş, Romania

A diagnostic curettage was made 3 days - 1 month prior hysterectomy. In the cases where at the biopsy there was one of the phases of the normal menstrual cycle, the patterns of the regenerative mucosa correspond to the evolution of the phase in that the curettage was done. In some cases indeed the freshly regenerated glands presented a multistratification and cystic dilatation characteristic for glandular hyperplasia.

In the cases with glandular hyperplasia at the first biopsy the hyperplastic character persisted during the regeneration. The initially atrophic endometrium showed a retarded or defective regeneration.

There is a correlated regeneration of the stroma and the glandular epithelium. The stroma is often edematous with loose structures. The stromal elements showed frequently an epithelium like arrangement at the surface of the endometrium - as it is visible also in granulation tissues with other locations. But the true epithelisation of the surface is realised by the proliferation of the epithelial lining of the remainent glands.

AUSWIRKUNGEN DER OVULATIONSHEMMER AUF DAS ENDOMETRIUM.
Holzner,J.H.,Dept.of Pathology, Univ.of Vienna, Vienna-Austria.

THE ENDOMETRIUM IN OVARIAN DYSFUNCTION.
Holzner,J.H., Dept.of Pathology,Univ. of Vienna, Vienna-Austria.

THE RESULTS OF HORMONE THERAPY ON ENDOMETRIAL STRUCTURE AND FUNCTION.

Holzner,J.H., Dept.of Pathology,Univ.of Vienna, Vienna-Austria.

DAS ENDOMETRIUM BEI PROLONGIERTER OESTROGENZUFUHR.

Holzner,J.H., Dept.of Pathology,Univ.of Vienna, Vienna-Austria.

PATHOGENESIS OF UTERINE TISSUE EOSINOPHILIA
Study of label elution and cell kinetics of radiochromium-labelled eosinophils and macrophages

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Dept. of Pathol. Med.Univ.,Pécs

In order to study uterine tissue eosinophilia in spayed rats treated with estrogens peritoneal exudate cells /eosinophils and macrophages/ were radiochromium-labelled in balanced salt solution or in medium TC 199 at 37°C for 60 minutes and first label elution examined /0-4 hours, at 4,20 37 and 56°C/. WBC /"Picoscale"/ and eosinophil counts, cell viability /dye exclusion test/, radioactivity, peroxidase and protein /Lowry/ level of the leucocytes, as well as of the cellular supernatants were determined. Released proteins were analysed for fractions by polyacrylamid-gel electrophoresis. On incubation at 37°C the number of non-viable cells gradually increased with a parallel rise in label and protein released from the cells. Morphological signs of cell decay were observed.

Following intravenous injection of labelled leucocytes into spayed rats blood, liver, spleen, kidney and uterine radioactivity were measured at 30,60 and 120 minutes/cpm/g wet tissue. Redistribution of the eosinophils was followed also by light microscopy. First the lung, later the liver and spleen showed accumulation of radioactivity, viz.of eosinophils.

CLINICAL EVOLUTION,MORPHOLOGICAL ASPECT AND CYTOGENETICAL STRUCTURE CORRELATIONS IN HUMAN MALIGNANT OVARIAN TUMORS.

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Cantacuzino Hospital, Laboratory of Pathology, Bucharest, Rumania

Morphological and cytogenetical structure of human malignant ovarian tumors was correlated with their clinical evolution.

There were investigated 3 vegetant epithelioma,1 arenoblastoma,3 malignant papilifere cystadenoma,1 undifferentiated epithelioma.

Inspite of their different morphological structure all tumors with a slow clinical evolution presented an intense fibrous reaction of peritumoral connective tissue accompained sometimes by inflammatory cells. The chromosome number distribution values were grouped in near diploid area and pseudodiploid or near diploid stemlines were found. In tumors with fast clinical evolution and metastatical dissemination the peritumoral immunological host reaction was decreased.These tumors presented wide ranges of chromosome number distribution with heteroploid stemlines.

It was concluded that morphological peculiarities of host versus tumor reaction as well as cytogenetical characters of tumor may indicate its biological evolution and proliferative capacity.

THERAPY OF OVARIAN DYSFUNCTION AND ENDOMETRITIS BY SEQUENTIAL TYPE NORSTEROID /OVANON/

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Dept.Obstet.Gynaec., Bajcsy Zs. Hosp., Budapest.

Sequential norsteroid treatment was used in 4o patients during 12o cycles. Distribution and results according to the clinical picture: Ovanon resulted in a regular menstruation in 2 patients with amenorrhoea 3 dysmenorrhoic patients became free of complaints, in one of them complaints on frigidity were eliminated.

In 4 sterile patients the drug has been administered on the principle of the rebound effect. Pregnancy occurred in one of them. The treatment was most seccessful in 19 patients with recurrent metrop.hem. having been subjected previously to various hormone therapies and repeated therapeutic curettage. Results were excellent in 6 cases of endometric bleeding due to postpartal and postabortal retention. In these cases the persistent postoperative bleeding did not respond any conservative treatment. Finally in 6 patients in whom contraciptives of nonsecuential type had to be discontinued because of side-effects / Breakthrough bleeding, emesis, headache, etc./ could be continued seccessfully by the sequential method.

The therapeutic effect was controled by continuous cytological tests and periodic endometrial biopsies. In the first half of the cycle cytology showed a physiological pattern. A greater amount of navicular cells was found in the secretory phase. During secuential treatment endometrial histology revealed always a typical proliferative pattern followed by the regular secretory phase.

PROGESTERONE EFFECTS ON NORMAL AND MALIGNANT ENDOMETRIUM.

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Memorial Hospital for Cancer and Allied Diseases, New York - USA.

The classical histologic effects of progesterone on the human endometrium will be briefly reviewed and discussed in relation to the variation of DNA and RNA synthesis occuring during the menstrual cycle and upon in vitro administration of progesterone to endometrial tissue suspensions. Two in vitro systems for the study of Endometrial Carcinoma will then be presented and progesterone effects on histology and the synthesis of nucleic acids achieved in vitro and in vivo on primary and metastatic endometrial carcinoma will be discussed and compared.

CHANGES OF THE ENDOMETRIUM FOLLOWING USE OF "ANTIOVULANTS" PROGESTINS.

Mr L. ORCEL, Melle H. GIORGI et Mme C. PALLUD

Service Central d'Anatomie et Cytologie Pathologiques Faculté de Médecine Saint-Antoine - 27, rue Chaligny 75571 PARIS CEDEX 12 (France)

The survey of endometrium samples taken from women who had been taking continuously various combination type preparations of œstrogens and progestins shows two different basic patterns : hypotrophy and dystrophy, probably linked with inhibition of F SH.R F and L H.R F. Hypotrophy seems to be induced more specially by high progestin doses. In several cases, it has been possible to define an œstrogenic or luteinic predominant "climate" variable with the preparation used and probably resulting from the direct effect of the drugs on the endometrium

In the same patient, the changes of endometrium do often vary during several consecutive menstrual cycles. Association of hypotrophy and dystrophy is the most distinctive feature.

EVALUATION OF 6300 ENDOMETRIAL BIOPSIES PERFORMED IN FUNCTIONAL, METHRORRHAGIC, AND OTHER UTERINE BLEEDINGS.

T. Sági, J.Nemes, Z. Zilahi.
Dept. Obstet. Gynes., Bajcsy Zs. Hospital.Budapest.

A total of 63oo endometrial biopsies were analysed during a 7-years period.
The bioptic material of postabortal retention, endometrial adenomata, or cc., hydatid mole, and tuberculous endometritis, altogether 3070 cases are discussed separately. Due to a so-colled functional bleeding 3230 histological examinations were performed. Findings were as follows: 1./ A various degree of glandular hyperplasia besides anovulatory cycle was frequentest /1085, 33.3 %/. 2./ The next important was the so-called hyperplasia glandularis cystica /336, 10.7 %/. The clinical picture was found from the age of 12 years up to the menopause, with a periclimateric prevalence. Postmenopausal bleeding could be interpreted solely by adrenocartical hyperplasia. 3./ Numerous histological findings revealed chr. endometritis /714, 22 %/. Here, the disturbance of the myoepithelial function of the endometrial vessels, due to an inflammation was thought to be responsible. 4./ A histological pattern of an impaired secretion phase was found in 5o4 cases /15.5 %/. Despite of the signs of the secretory phase on the mucosa, the bleeding is delayed. Deficient progesterone production, the slow regression of the corpus luteum, or, though the corp.luteum reached full maturity a prolonged decrease of progesterone production could be concluded. The mucosal pattern observed in case of cysts of the corp.luteum may be ranked here, too.

HORMONBEHANDLUNG DES ENDOMETRIUMCARCINOMS UND SEINER VORSTUFEN.

Schmidt-Matthiesen,H., Frauenklinik d.Johann Wolfgang Goethe Universität, Frankfurt-GFR.

ENDOMETRIALE BLUTUNGEN UND HAMOSTASE IN ABHÄNGIGKEIT VON HORMONEINFLÜSSEN.

Schmidt-Matthiesen,H., Frauenklinik d.J.W. Goethe Universität, Frankfurt-GFR.

ENDOMETRITIS INTERSTITIALIS.

Scholz Magda, Váradi,I., Weil Emil Municipal Regional Hospital, Dept.of Pathology and Dept.of Obstetrics and Gynaecology I., Budapest-Hungary.

Endometritis interstitialis is an illness of the endometrium where the degeneration of the interstitium is the most emphatic. According to 500 endometrium-material examinations with such diagnoses over 15 year period, it was found primarily during the praeclimactiv age /39-45/. Its symptoms generally include irregular bleeding, in subacute form with stroma oedema, lymphocytaer cell reaction with more or less intense bleeding. It is more often found in patients with several previous abortions and following therapy with oral contraceptives. In 20% of the cases it is complicated by hyperplasia glandularis of the endometrium and joins the hormone producing ovarian tumors or endometriosis. As can be seen from the above endometritis interstitialis cannot be considered a simple inflammatory illness, but rather a result of an endocrine malfunction.

KLINISCHER EINSATZ DER HORMONTHERAPIE BEI GUTARTIGEN FUNKTIONSSTÖRUNGEN.

Stoll,P., Frauenklinik d.Univ.,Mannheim,GFR.

Die Behandlung mit Sexualhormonen ist als Behandlung mit stark wirkenden Arzneimitteln anzusehen.Eine klare Diagnosestellung und eine strenge Indikation sind daher Voraussetzung für die Behandlung.Neben einer gezielten lokalen Wirkung auf die Erfolgsorgane ist immer auch mit einer komplexen allgemeinen Wirkung zu rechnen,welche die gesamte endokrinische Steuerung, den Stoffwechsel sowie die somatische und psychische Entwicklung betrifft. Um die Gesamtheit der Wirkungen zu erkennen, ist der Einsatz zahlreicher Untersuchungsmethoden erforderlich, deren Bewirtung auf der Waage medizinischer Erkenntnis Schwankungen unterliegt.Die Behandlung kann daher niemals in einer einmaligen Verordnung bestehen,sondern muss fortlaufend kontrolliert werden,wobei sowohl die Dosis als auch die Zusammensetzung des Hormonpräparates immer wieder neu erwogen werden muss. Die Einflussfaktoren,die den Hormoneffekt im Einzelfall beeinflussen sind:biologische Wirksamkeit der Hormone,hormonale Ausgangslage der Patientin,individueller Metabolismus,individuelle Ansprechbarkeit der Zielzellen,Applikationsart und Zeit.Hinsichtlich der Applikationsform unterscheiden wir: Implantation,Injektion,perorale Behandlung,lokale Behandlung,vaginale Applikation,rectale Applikation.Hinsichtlich Einsatz und Wirksamkeit unterscheiden der Erfolgsorgane eine Substitution,eine Stimulation und eine Bremsung übergeordneter Funktionen.

INFLUENCE OF OVARIAN HORMONES ON THE FINE STRUCTURE OF ENDOMETRIUM WITH SPECIAL RESPECT TO THE ROLE OF LYSOSOMES.

Z.Szarvas
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Investigations of the last years shown that the behaviour of lysosomes of the endometrium depends to a great extent on the timely hormonal influences. The number of lysosomes increases under the influence of estrogens. The presence of lysosomes in the epithel cells of endometrium expresses morphologically the estrogenic influence on the endometrium and it is one of its important manifestations. In our research the lysosomal kind of the structures has been verified by acid phosphatase reaction. The humber of lysosomes is reduced and their integrity changed as a result of the effect of progestational treatment. It can be established that ovarian hormones have an opposite effect on lysosomes. The estrogens stabilize the lysosomal membrane while the progesterone affects the permeability of lysosomal membrane having the result that the hitherto inactiv enzymes get into the cytoplasm and become activised.

CEREBRAL INFARCT,PULMONARY EMBOLISM AND NONBACTERIAL,NONRHEUMATIC ENDOCARDITIS ASSOCIATED WITH ORAL CONTRACEPTIVE, A CASE REPORT.

E.Thomas, A.M.House - General Hospital,St.John's NFLD,Canada - Memorial University, St.John's,NFLD, Canada.

A 31 year old white female suddenly became semicomatose and unable to speak on February 23rd,1973. She was on oral contraceptives for seven months. She had been in good health before except for migrainous headaches. No other medications had been given. She was admitted into the hospital on February 23,1973 in a semicomatose state with aphasia, right hemiplegia and right homonymous hemianopsia. Left carotid angiography showed occlusion of the left middle cerebral artery. She was treated with steroids. There was improvement for 2 weeks followed by a hypotensive episode. She died on March 19,1973. - Autopsy showed extensive cerebral infarction of left temporal lobe, massive pulmonary embolism and nonrheumatic, nonbacterial early endocarditis of mitral valves with vegetations. While cerebral ischaemia and pulmonary embolism have been described in many women using contraceptive pills, autopsy studies of nonrheumatic nonbacterial endocarditis have not been reported in world literature.

CHANGES OF ENDOMETRIUM DURINT CONTRACEPTIVE TREATMENT.

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1st Dept.of Obstetrics and Gynecology and 2nd Dept.of Pathology, Semmelweis Medical University, Budapest-Hungary.

A total of 1004 women were given for 11.628 cycles contraceptive tablets of different composition. Combined preparations containing 2.5 mg progestogens and 100 ug. estradiol caused severe atrophy of the endometrium, reduced estrogen production and induced lasting side-effects. The combined preparations cause mostly endometrial edema, which is followed after a certain time by edema-sclerosis. The sclerosis may result the irreversible damage of the fine structures of endometrium. The ratio and temporal occurrence of the damages depend on the quantitative and qualitative composition of the contraceptive pills and also on the hormonal status and stage of development of the uterus.

Histology of the endometrium differs considerably from the above pattern in patients on sequential therapy. The sequential method developed by the authors possesses considerable advantages.

THE HISTOLOGICAL PICTURE OF ENDOMETRIUM-MATERIAL FOLLOWING PROLONGED USE OF ORAL CONTRACEPTIVES.

I.Váradi, Magda Scholz,Weil Emil Hosp.,Dept. of Obst.and Gynec.I.,and Dept.of Pathology, Budapest-Hungary.

Over a 5 year period we found pathological bleeding after prolonged use of oral contraceptives/Bisecurin and Infecundin/ in 200 cases.In those cases where conservative methods were unsuccessful,we performed curettage partly for therapeutical,partly for diagnostic reasons.After histological examination in 90% of the cases we detected endometritis interstitialis which is often joined by anomalies of the proliferative and secretive phases,the infections were more or less of a haemorrhagical nature and are paired with subacute and large-scale stroma edema.The amount of mucopolysaccharide detected in the endometrium by various methods increases,the reticular and elastic fibre content of the stroma decreases,the stroma suffers mucoid degeneration.The endometrium becomes similar to the hyperproduction of the glandular epithel cells,to the cystical degeneration of the glands and to the regressive changes of the epithel cells.The mitochondrial and Golgi apparatus and ultrastructure of the glandular epithel suffers.The remaining 10% was observed to be hyperplasia glandularis.In the endometrium-material taken following a pause of several months in the contraceptive therapy,the normal histological and histochemical conditions of the endometrium were observed.

CHRONIC PULMONARY DISEASES EXCLUDING TBC AND TUMOUR

Organized by

DIACONITA, G.

Invited lecturers

BALOGH, J.
DIACONITA, G.
ESKENASY, A.
GALY, P.
GIESEKING, R.
HARTUNG, W.
HOLMA, B.
MISKOVITS, G.
OTTO, H.
ROUSSEL, Ph., DEGAND, P., LAMBLIN, G., HAVEZ, R.
STERNBY, N. H.
YESIPOVA, I. K., PHEDOTOVA, O. P.

"ALVEOLAR CONTRACTILE CELLS". ULTRASTRUCTURAL AND IMMUNOFLUORESCENCE STUDY ON RAT LUNG.

A. Assimacopoulos, A. Zwahlen, C. Irlé, G. Majno, Y. Kapanci

Department of Pathology, Geneva, Switzerland

Fibrillar bundles of "contractile" type are described in interstitial cells of alveolar septa. Normal rat lungs were fixed by perfusion for EM studies and fresh cryostat sections were treated with specific human anti-actin-serum obtained from a patient with chronic aggressive hepatitis (Gabbiani et al.,1973). "Contractile cells", different from usual smooth muscle cells, are demonstrated in the thick portion of the air-blood barrier and around the pre- or post-capillary vessels. They have features of fibroblasts and possess intra-cytoplasmic bundles (0.25-0.50 μ thick) of parallel fibrils (32-81 Å Ø) beneath the plasmalemma. These bundles appear stretched between two basement membranes and sometimes between connective tissue fibers and a basement membrane.

Immunofluorescence studies reveal numerous actin-containing cells in the alveolar septa.

It is postulated that these cells might be responsible for the contraction of lung parenchyma in hypoxic media, as already demonstrated in vitro. Their privileged situation in the walls of sacculi argue in favour of their participation in the ventilation-perfusion auto-regulation. Their possible role in hypoxic pulmonary hypertension is discussed.

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LUNG ANGIOARCHITECTONICS IN CHRONIC HUMAN AND EXPERIMENTAL PULMONARY HYPERTENSION.

J.Balogh, Dept.of Pathology, Balassa Hospital Szekszárd, Hungary.

A lot of publications deals with the architectonic of major pulmonary artery branchs in chronic pulmonal hypertension. Our studiens discuss the perfusional, that is the final part of pulmonary artery, too.

We compared the chemical lipid structures of major pulmonary branches with the alterations in artery's architectonic, observed in different sectors. - The material studied originated from human secunder pulmonary hypertension cases, following destruction of lung parenchyma /emphysema, pulmonary fibrosis, silicosis, post-tuberculotic lung, etc./ In our experimental studies we induced pulmonary fibrosis and consecutive hypertension by paraguat intoxication, completed by measuring of pulmonary arterial pressures. Beside the determination of quantitative conditions we applicated radio-microangiographic studies too, by modified Hill-s metnod. Our paper deals with: 1/ morphologics of arteriolar-capillar segment; 2/ connections of major and minor vessels alteration; 3/ relation of pulmonary vessels lipoidosis with the vessels wall and histochemical conditions; 4/ the same and different appearences of normal gerontologic vessel alterations and hypertonic pulmonary vessel damages.

RARE PULMONARY COMPLICATIONS IN CHILDREN WITH ACUTE LEUKEMIA FOLLOWING TREATMENT WITH CYTOSTATICS

Börzsönyi, M., Lapis, K., Schuler, D., Machay, T. and Görgényi, Á.

1st Institute of Pathology and 2nd Clinic of Pediatrics, Semmelweis Medical University, Budapest, Hungary

The "Busulfan lung syndrome" developing in adults with leukemia /Oliner et al.,1961; Leake et al., 1963/ and the fibrosis of the lung in patients treated with Melphalan /Colding and Chakera, 1972/ are well known.

Examining cases of acute leukemia in children rare pulmonary complications were observed in the state of haematological remission following combined treatment with Vincristine, Rubidomycin, 6-Mercaptopurine, Metothrexate and Asparaginase as fatal mycosis of the lung, alveolar proteinosis, fibrosing alveolitis resp. the initial and not fatal form of the latter. The clinical symptoms were characterized by fever, cyanosis, tachypnoea and bronchitic moist rales. The chest X-ray revealed small focal infiltrations, "butterfly"-like spotted shadows and hilifugal, reticular shadows. The mycosis of the lung was produced by Candida albicans. The clinical picture involving the fibrosis of the interalveolar septa is named by the term iatrogenic fibrosing alveolitis.

Attention is called to the possibility of easing clinical symptoms by stopping treatment with cytostatics early after complications

PULMONARY CONGENITAL ALVEOLAR DYSPLASIA ASSOCIATED WITH MICROLYTHIASIS.

L.T.Caluser, Dept.of Morphopathology of the Faculty of Medicine, Cluj, Romania.

A boy aged 3 died with the clinical diagnosis of meningoencephalitis. Post-mortem examinations revealed dense lungs with a positive docimatic test. Microscopically, areas of young connective tissue surrounded by pulmonary tissue with enlarges alveolar septs an epithelium partly desquamated were noticed. In other areas alveoli were larger and lined with cubo-columnar non-functional epithelium. In connective areas, lumen and alveolar walls numerous small calcium concretions were found.

This association between pulmonary congenital alveolar dysplasia, described by Mac Mahon, with pulmonary microlythiasis enriches morphogenetical knowledge on calcium concretions in the lungs.

INTERSTITIAL DESQUAMATIVE PNEUMONIA

H. Csermely, K. Szirmai, A. Pintér
Department of Pathology, MAV Hospital
Budapest, Hungary

While in the literature interstitial desquamative, lymphocytic, giant cell, cholesterol, obstructive pneumonias and diffuse interstitial fibrosis with alveolitis are dealt with as separate entities, the authors come to the conclusion that all these pathological pictures, except cholesterol and obstructive pneumonias, are to be classified as a common pathological group. Inflammation of the air-blood membrane, presumably of autoimmune origine, is to be regarded as primary damage to wich desquamation in various intensity, lymphocytic infiltration, fibrosis and finally sclerosis,/Hamman-Rich/ may join.

The histological characteristics named above are also encountered in the course of the morbid process together. The desquamation is closely connected with the syncytial giant cell formation. If this reaches a high degree the denomination "giant cell interstitial pneumonia" is justified.

Cholesterol, lipid and obstructive pneumonias, furthermore pulmonary alveolar proteinosis are excluded from this group being the inflammatory proliferation of the interstitium in these processes secondary.

CHRONIC CELLULAR AND VASCULAR CHANGES IN LUNG SUPPURATIONS

Diaconita,G.
Instit. of Tuberc. Depart. of Pathol. Bucharest - Romania

Chronic cellular and vascular changes occuring secondarily in lungs with suppurative processes are presented. Literature data and personal research carried out in 2oo cases who underwent pulmonary reseactions for chronic bronchopulmonary suppurations were used. Chronic cellular changes were studied in pulmonary mesenchymal,inter and intralobular, parieto-alveolar and peribronchovascular areas, and study of the vascular changes incuded smal and middle vessels. The reactions of mesenchymal elements were characterized by: 1. Cellular proliferations which reflect histogenetically and immunogenetically the way and the degree of challenging of the reticulo-endothelial system, as well as the intensity of resorption processes. 2.Cellular differentiation was of various types: reticuloplasmoblastic cells,plasma cells with obvious pyroninophilia, hystiocitar,fibroblastic,macrophagic or eosinocitic elements. Recent research showed that proliferation and cellular intralobular changes have in most cases an immunomorphologic component which becomes manifest during sensitization processes. The chronic vascular changes most frequently encountered were of ischemic type,as well as processes of perivasculitis provoked by perivascular proliferation and adventicial reticular cellular differentiation.

EXPERIMENTAL BASES OF CHRONIC LUNG DISEASES

Eskenasy Alex.
Div.Pathology Tbc Institute Bucharest Romania

The importance of prolonged and repeated penetration of pathogenic agents - antigenic and non antigenic - on the air ways and on the functional circulation with induction of ite - rative and intricated reactions of immune, inflammatory and regenerative type, with cel lular, vascular and fibrous componeats, are discussed in the lecture.

The prolonged innalation of noxious agents as well as the bronchial onstruction led to parenchymal lesions. The induction of repeated hypersensitive reactions in the sensitized lung produced bronchial and alveolar diffuse cellular processes, with fibrosis by redundant synthesis of mucopolysaccharides in the cellularized structures, basic components of chronic lung diseases. Isologous, hete rologous and modified antigens enhanced the action of germs and antigens, drawing the cellularization of alveolar walls, and the immune vasculites with consecutive circulatory changes, in repeated penetrations on respira tory or parenteral ways. The sensitized lung also represented a reacting substrate for heterologous antigens. The processes, initially aerogenic, induced and maintained the inter- and intralobular cellular reactions with fibrosis, air spaces occlusion, and chronic lung disease formation.

PNEUMOCONIOSIS CAUSED BY THE MECHANICAL HATCHING OF POULTRY

Fáber, Károly and Geiger, Éva
Municipal Hospital Named "Weil Emil"
Budapest, Hungary

The lecturers will introduce the clinical, pathological and histological examinations of a 43-year-old female patient. We detected pneumoconiosis in the patient. Besides the grain dust, the organic dust found during the mechanical hatching of poultry also played an important part in causing the lesion of the lungs. The inhalation of the poultry down in the hypersensitive organism produced the following lesions: pneumonia interstitialis acuta et chronida disseminata; pneumosclerosis disseminata; hepatitis granulomatosa; lymphadenitis chronica fibrosa, etc. The lesion of the lungs, caused by cor pulmonale led to the death of the patient.

PSEUDO-TUMORAL CHRONIC PNEUMONIAS: ANATOMIC AND BRONCHOGRAPHIC STUDY

GALY P., Bronchopneumologic Institute, CARDIOVASCULAR AND PNEUMOLOGIC HOSPITAL LYON-BRON (France)

From an anatomic study of sixteen specimen of chronic pneumonia who have been obtained by exeresis performed with the false or suspected diagnosis of bronchial carcinoma : the conclusions are : pulmonary fibrosis of various types - cholesterol alveolitis-pulmonary post inflammatory and atelectatic atrophy-lymphohistiocytary nodules - Slight wideming of main bronchi and stenosis of distal bronchi (polystenotische atelektase).

The state of main and distal bronchi may be in vivo appreciated by bronchography.

Bronchographic study of 41 cases of chronic or slowly resolutive pneumonia was made with comparison of the shadows seen by bronchography along the evolution of bronchial segmental carcinoma/.

It is possible to find peculiar distinctive caracteristics : stenosis of the main bronchi in carcinoma- wideming in pneumonia.

Possibility is emphasized of main bronchi radiological stenosis in chronic pneumonia, (7 cases) and of bronchial distal impregnation in bronchiolo-alveolar carcinoma (4 cases).

ULTRASTRUCTURAL ALTERATIONS OF THE BRONCHIAL MUCOSA IN CHRONIC BRONCHITIS.

Gieseking, R., Path.Inst.d.Universität, Münster-GFR.

FUNCTIONAL IMPLICATIONS OF CHRONIC BRONCHITIS AND EMPHYSEMA

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Pulmonary emphysema should be differentiated. Its types are the result of a different pathogenesis. Chronic bronchitis very often is associated with emphysema. It may be the cause of emphysema, while in other cases it seems to develop secondarily as a complication of emphysema.

The use of histomechanical post-mortem function tests is a good means to demonstrate functional disturbances, e.g. static and dynamic compliance, intrapulmonary gas volumes, resistance, maximum expiratory flow, and ventilatory distribution disorders. The data in most cases can be easily compared with the results of similiar clinical tests.

By a combination of such histomechanical parameters with morphology, particularly using the GOUGH large-section technique, the pathogenetical basis of emphysema can be elucidated and the type and degree of structural alterations correlated with typical functional implications and prognosis.

THE MORPHOLOGICAL PICTURE AND ETIOLOGY OF CHRONIC PNEUMONIA IN RESECTED LUNGS

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Resected lungs were studied of 185 patients with lobectomy or pulmonectomy for chronic pneumonia from 1965-1972. The sex-ratio was 3,4:1 on behalf of men. There was a broad peak in the age-group of 54 to 64, with an average age of 47,6 years.Seat of the lesion was in 121 cases the right, in 64 cases the left lung, with highest frequency in the right upper lobe (39 cases) followed by the right lower lobe and left lower lobe (36 cases each).The more extensively the histological study was carried out, the more polymorphous was the histological picture.
Chronic carnificating pneumonia and chronic interstitial inflammation alternated with areas of fibrosis and foam-cell-pneumonia. Alveolar rests and proliferating bronchioli usually showed high cubic epithelium. Strict typing of chronic pneumonias according to the histological picture was not possible.
One third of the cases presented bronchiectases. In 16 patients foreign bodies (gunshot wounds and aspirated foreign bodies) were of causative significance, one case was a through-and-through-wound, an other an impalement injury, and two cases presented honeycombe-lungs. 6 patients showed fungus infection of abscess cavities. Bacteriological examination revealed a preponderance of staphylococci,followed by streptococci, enterococci and E.coli as the most important germs.

SOME MORPHOPATHOLOGICAL EFFECTS OF INHALED PARTICLES IN THE RESPIRATORY TRACT.

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LES RÉACTIONS IMMUNOMORPHOLOGIQUES PULMONAIRES AU COURS DES HÉPATHOPATHIES CIRRHOGÈNES.

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On a étudié les modifications histologiques des diverses zones des poumons des 30 cas de hépathopathies cirrhogénes chez les enfants et jeunes, sans complications infectieuses. On a étudié aussi la morphopathogenese des lésions pulmonaires des divérses hépathopathies cirrhogenes /toxiques,cholestatiques, vasculaires/ sur 200 rats blancs.On a constaté l'apparition des certains réactions immunomorphologiques: hyperplasies cellulaires alvéolaires, proliferations lymphoplasmocytaires pyroninophiles périvasculaires vasculites pulmonaires et des pnéumonites, processus de fibrose, parfois des alveolites. Les formations lymphoides péribronchiques présentent aussi des modifications réactionelles. Les réactions pulmonaires sont intensifiée quand on a associé la splénectomie et diverses agents pathogenes. On a établit des correlations entre l'intensité des réactions des éléments mésenchymateuse pulmonaires et ceux du foies et des autres territoires du SREH. Dans les formes agressives de hépathopathies chroniques avec modifications de valeurs des Ig on a constaté souvent des réactions immunomorphologiques pulmonaires,aussi bien que des autres organes.

ULTRASTRUCTURAL STUDY OF TWO CASES OF VIRAL INFLUENZALPNEUMONIA IN HUMANS.

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The lung samples were taken immediately after death while the subjects were still under perfusion and ventilation. Our study was concentrated on the changes of the lung parenchyma and the virus particles.

I-There are 3 types of lesions: 1°-Lytic changes of the endothelial and epithelial cells, 2°- Changes of the septal connective tissue characterized by edema, fibrin deposits, elastic dystrophy, onset of fibrosis with multiple microfibrils of tropocollagen and prominent alterations of vascular and epithalial basement membranes, 3°-Changes of the alveolar lumen filled with edema, fibrin deposits, phospholipidic membranes and necrotic debris.

II-Virus like particles measuring 1,000 A and showing a nucleoid and an envelope were seen in the septal connective tissue and the alveolar lumen. They were sometimes localized on the cell surface and on top of the microvilli. Virus like particleswere also observed within the cytoplasm with different morphological features.

THE EFFECTS OF UNILATERAL PULMONARY ARTERY OCCLUSION ON THE LUNG CIRCULATION OF THE DOMESTIC FOWL.

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The knowledge of the avian lung circulation is small. The effects of unilateral pulmonary artery occlusion /UPAO/ have been extensively studied in mammals. Whether the avian lung will increase its systemic,bronchial circulation and what are the hemodynamic and electrocardiologic changes after UPAO? We tried to find answers using domestic fowl as experimental animal.

Left thoracotomy was performed under local anesthesia and left pulmonary artery was occluded by silver clips.The animals were studied before UPAO and after various postoperative intervals using morphologic,hemodynamic, and electrocardiologic methods.

The systemic vascularity of the left lung increased. Blood within the bronchial vessels was,however, probably unable to receive or give gases because of the changes in the air-blood wall. Morphologically three months after UPAO the left lung resembled emphysematous mammalian lung. Cardiac output and stroke volume increased, peripheral vascular resistance decreased after UPAO. ECG-changes were small and vanished within 2 - 3 days.

THREE ASPECTS OF CYTOMEGALIC INCLUSION-BODY DISEASE IN THE PULMONARY PATHOLOGY

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The occurrence of lung localisation in cytomegalovirus infection /CY/ is rare. Author in his own autopsy material found 27 out of 185 infant cases with CY, among that were 3 with lung CY.

The lung CY is mostly 1. a part of generalised CY. It is frequent in newborns and infants. This lung localisation doesn't lead to a fatal prognosis. 2. In cytomegalovirus pneumonitis one finds alveolar and interstitial exsudate beside the giant-cells. It is the single serious lung disease caused by the cytomegalovirus. A rare form, wich appears mostly in adults. 3. CY is often together with various lung diseases: transplanation pneumonitis, lung- mycoses, mucoviscidosis and pulmonary manifestations of hematological, immunodeficient and neoplastic diseases. In prematures the most frequent apperance is together with pneumonystis pneumonia /PP/. In author's own material among 26 CY cases in 18 found also PP and analyses the possibile causes of this syntropic occurrence.

Author observed also an adult lung CY case together with lymphocytic interstitial pneumonia wich progressed lung fibrosis. These two lesions are due to the patient's immunodeficient state.

SO-CALLED ASBESTOS BODIES IN HUMAN LUNGS AT AUTOPSY (FREQUENCY AND SIGNIFICANCE)

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Lung tissue obtained at random necropsies from 234 persons aged from 30 to 88 yrs was examined for the occurrence of so-called asbestos bodies by means of the digestion method of GOLD and KERR. In 22 cases (9,4%) morphologically typical asbestos bodies were found. An increased incidence of these bodies in lungs of persons with diverse malignancies in comparison to persons without neoplasms could not be ascertained in our series. The quantity of so-called asbestos bodies in our positive cases amounted to about 1.600 to 1.800 per 1 g dried lung tissue. However, nearly 100.000 to 120.000 asbestos bodies per 1 g dried lung tissue were found by the same method in preserved lung tissue of a 58-yr-old man with an asbestosis. The great variation of the frequency of so-called asbestos bodies in human lungs at autopsy (0 to 100%) which are to be found in 31 reports of the literature is interpreted by the economical structure of the collection district and by the different examination methods. The fact is stressed that morphologically identical "asbestos" bodies can also be induced by inhalation of filamentous materials other than asbestos. As long as simple methods are not available for distinction of true from false asbestos bodies, the presence of these bodies in human lungs as sign of a significant previous asbestos dust inhalation should be critically considered.

CHRONIC, OBSTRUCTIVE PULMONARY DISEASES.

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MORPHOLOGY AND PATHOGENESIS OF DESTRUCTIVE EMPHYSEMA.

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Destructive emphysema is a condition which can only be demonstrated in a distended lung. The best way to demonstrate emphysema is the technique of paper mounted sections according to Gough. This technique in a modification is shown in a five minute-film. Under anatomical aspects the centrilobular emphysema, the panlobular emphysema and the emphysema of the empty lobule can be distinguished. Under pathogenic aspects there are three types of emphysema: 1/ The primary obstructive emphysema; 2/The kinetic emphysema; 3/ The emphysematous lung sclerosis.

The primary obstructive emphysema is the result of postobstructive overdistension. It is always of panlobular type. The kinetic emphysema develops at certain given frontiers of elastic inhomogenity. Emphysematous lung sclerosis is identic with honey comb lung. This alteration is not to be overformed by obstruction. Development of emphysematous lung sclerosis can be observed by lung biopsy. Asbestosis and sclerodermia e.g. are conditions which lead to emphysematous lung sclerosis.

BIOCHEMICAL FEATURES OF BRONCHIAL SECRETION FROM CHILDREN WITH CYSTIC FIBROSIS.

Roussel,Ph.,Degand,P.,Lamblin,G.,Havez,R.

By washing sputum with 0.9% sodium chloride, it is possible,after centrifugation,to separate two main phases:the soluble part of mucus and an insoluble part containing cells and a fibrillar structure.Bronchial fibrillar mucus may be desagregated and solubilized by proteolysis or reduction.Reduction allows the subsequent identification of five molecular groups: proteins antigenically related to serum proteins;proteins typical of secretions such as kallicrein,bronchotransferrin,Y_A-immunoglobulins with the secretion piece,lysozyme,and a trypsin-inhibitor; lipids whose composition is closed to lung surfactant;nucleotidic components;and mucins. Mucins are glycoproteins with a chemical composition similar to blood group substances and most of them have a blood group activity.Bronchial glycopeptides can be obtained by proteolysis of bronchial fibrillar mucus and fractionated on ion-exchange chromatography according to their acidic characters. This procedure was applied to sputum from 50 children with cystic fibrosis.Contrary to what was observed in other bronchial diseases,results obtained with cystic fibrosis sputum were very homogeneous:most of the glycopeptids are acidic.Purification of bronchial mucins from children with cystic fibrosis was achieved.These mucins contain simultaneously N-acetylneuraminic acid residues and sulfate groups.Structural works are actually in progress.

ON THE RELATION THE ISOLATED SPINAL EPIDURAL HAEMORRHAGE AND THE HYALIN MEMBRANE DISEASE OF THE PRAEMATURE INFANTS

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Haemorrhage of the central nervous system may be found often at the autopsy of praemature infants. The intraventricular haemorrhage attributed to the anoxic damages /Frederick and Butler/ was observed occuring mainly in the lower birth weight infants/under 1200g./, and the isolated epidural spinal haemorrhage attributed to the mechanical factors/Towbin,Walter and Tedeschi/ could be found mostly in the higher weight infants /more than 1700 g./ 3/5 part of the praemature infants with isolated spinal haemorrhage was suffered from the hyalin membrane disease too. The average weight of these is 2060 g. although the hyalin membrane disease is the illness of the low weight infants. As far as the pathogenesis of the hyalin membrane disease is concerned, the role of the lymphatics is emphasized. The respiratory movements of the infants suffering from the isolated spinal haemorrhage are inert. But the most important factors in keeping the pulmonal lymp flow are the respiratory movements. By this way the isolated spinal haemorrhage may be an important fact revelated to the developing of the hyalin membrane disease in praemature infants with higher birth weight.

THE DIAGNOSTIC VALUE OF OPEN LUNG BIOPSY

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At 72 patients, 51 males and 21 females there was performed pulmonary biopsy through thoracotomy exclusively with a diagnostic aim. There were sectioned 1-3 fragments of lung, most frequently the right lung. These patients presented nodulary or reticulonodulary radiologic features which could not be clarified nosologically through other investigation methodes, thoracotomy being the last.

The rezult gave a certain diagnostic in 54 cases (75%), a informativ diagnostic, relatively useful in 10 cases (13,8%) and 8 cases were negative (11,2%).

From the diagnosticated diseases we mention: broncho-alveolar carcinomas, sarcoidosis, silicosis, primary pulmonary sclerosis, leiomiomathosis (bronchiolar emphysema), histiocytosis X, alveolar proteinosis, microlithiasis, idiopathic pulmonary hemosiderosis i.e.

In the cases with an incomplete diagnostic there were found not characteristically alveolar and septal sclerosis of a secondary origin.

It is discused the usefulness of the open lung biopsy in relation to sex and age.

PULMONARY EMPHYSEMA IN AN UNSELECTED AUTOPSY SERIES.

Sternby,N.H., Dept.of Pathology,General Hospital, Malmö-Sweden.

HISTOPATHOLOGY OF RESPIRATORY BRONCHIOLES IN CHRONIC NON-SPECIFIC PNEUMONIA

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Patris Lumumba Peoples' Friendship University
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Micrometric findings show that muscle cells in walls of respiratory bronchioles of the first order normaly constitute 50-60 per cent of the wall thickness in persons below 30 years. With age the index does not change significantly but in chronic bronchitis it rapidly falls. Judging by the parallelism between the index, the parameters characterising acinus shapes, and the ventricular index, changes in smooth muscles of respiratory bronchioles play the key role in development of emphysema and cor pulmonalae. Electron microscopy and histological techniques permitted to demonstrate that the extension of smooth muscles leads to their hypertrophy which is rapidly followed by atrophy and solerosis. The starting mechanism of such changes in lungs is probably the disturbance of the aerodynamics.

PATHOLOGY TODAY AND ITS TEACHING

Round table

Organized SYMEONIDIS, A.

Moderator DUSTIN, P.

Invited participants

BOLCK, P.
BOUTEILLE, M.
DUSTIN, P.
GIORDANO, A.
HOLZNER, J. H.
JELLINEK, H.
MOSTOFI, F. K.
PAPILIAN, V. V.
PLANK, J.
SEROV, V. V.

COMPUTER APPLICATION IN PATHOLOGY

Organized by

BECKER, H.

Invited lecturers

A. CLASSIFICATION AND NOMENCLATURE
SOBIN, L. H.
WELLS, A. H.

B. DATE PROCESSING IN PATHOLOGY
BALOGH, J.
BECKER H.
van der ESCH, E. P.
ROETTGER, P., WINGERT, F., FEIGL, W., GRAEPEL, P.
GROSS, U. M., RIES, P., MATAKAS, F.
THIERBACH, R.

C. EPIDEMIOLOGICAL PATHOLOGY AND DATA PROCESSING
BAUMANN, R. P., GLOOR, E., TISCHER, O.
JACOB, W.

D. STATISTICAL EVALUATIONS
ZSCHOCH, H., KLEMM, P.

ELECTRONIC AUTOPSY DATA PROCESSING OF CHRONIC CARDIO-PULMONAL CASES.

Balogh,J., Dept.of Pathology the Balassa Hospital, Szekszárd - Hungary.

Macroscopic and microscopic data of 300 patient died because of pulmonary hypertension were processed.
Principal data analysed and results obtained were as follows:

1./ Variation curves of nucleal sizes from right and left ventricle's muscle cells show regular alteration from control cases.

2./ In case of coexistant pulmonary and peripheric hypertension the single curves show differences too.

3./ It is a pregnant correlation between macroscopic-microscopic lesions of pulmonary vessels and the former date of right ventricle.

4./ A correlation can be find between the localisation and increase of hydrolytic enzymes and calibre alterations of vessels.

5./ Decrease of vessel wall's dehydrogenics enzymes correlates with qualitative damages of vessel's musculature.

6./ The accomodation's decompensatory end-stage of pulmonary circulation is nearly matematically determinable by former date.

COMPARISON OF BIOPSY MATERIAL FROM TWO INSTITUTES OF PATHOLOGY; ITS INFLUENCE ON TERMINOLOGY AND CLASSIFICATION

Baumann R.P., Gloor E., Tischer O.

Institut neuchâtelois d'anatomie pathologique, Neuchâtel; Institut universitaire d'anatomie pathologique, Lausanne; Suisse.

A brief description of the system of data processing used (manual coding and automated linking with SNOP-code for biopsy and autopsy diagnoses). A statistical analysis of numerous parameters (age incidence, frequence of some diagnoses, frozen sections, etc.) is carried out and significant differences between the two institutes (university and non university) are presented. The number of cases treated are about 50'000 (Lausanne) and 18'000 (Neuchâtel). Special attention is given to the cases with diagnostic or technical problems, and also to the contribution of external experts or specialists.

The authors examine personal, technical and other individual differences in the diagnostic language. They try to determine the efficacity and usefulness of their list of preferred terms which is the classification used for computer coding. They hope, therefore, that data processing contributes to a better understanding of our methodes of observation and interpretation of diseases.

EXPERIENCES WITH A TEST-STAGE FREE-TEXT PROCESSING SYSTEM IN PATHOLOGY USING DISPLAY TERMINALS

Becker, Hans
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Author gives a full description of a system for computerization of pathology reports in German clear text based on a thesaurus which has been compiled by incorporating more than 40 000 entry words.These words have been encoded according to the Systematized Nomenclature of Pathology thus representing a classified system with a logical structure.Text input is performed on a key - board with CRT display.Automatic analysis of reports is executed in a 128 k core storage computer with external random access bulk stores following FORTRAN written programs. Evaluations are initiated by a VDU using a very simplified retrieval language which enables the pathologist himself to specify questions in an on-line dialogue. The system has been in test stage operation for two years.Up to now 10 000 biopsy reports and 1 000 autopsy protocols have been analyzed automatically,stored, and retrieved by numerous questions combining up to 9 variables. Experiences gained give definite hints concerning suitable input media, structure of a thesaurus on different levels of text analysis,and indications to the function of a centralized pathology register.

A GENERATIVE MODEL OF PATHOLOGIC PROCESSES AND ITS USE FOR SIMULATED DIAGNOSIS.

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A general model is described whereby pathological pictures are generated according to statistical production rules within a given nosological structure. Simulated case studies are then used for diagnostic recognition performance and learning evaluation. The influence of observation errors, input classification and prior experience of the recognition system are determined.

HISTOLOGICAL,MORPHOMETRICAL and STATISTICAL INVESTIGATIONS IN LIVERS and LUNGS OF RATS AFTER THERMOCOAGULATION OF THE THORACIC DUCT BEFORE THE LEFT ANGLE OF JUNCTION.

H.Cremer,+N.Müller,R.Nienhaus and J.Tantow
Institute of Pathology and Dept. of med. Dokumentation,Statistik and Datenverarbeitung der Medizinischen Fakultät,University of Bonn,GFR.

In the liver we observed during the first 10-15 days a dilatation of the Disse and Mall spaces together with an ectasia of the lymphvessels within the portal tracts and of the lymphvessels which accompany the liver veins.The hepatocytes exhibit a vacuolization of the cytoplasm,but no necroses could be detected.On measuring the wet weights and dry weights we found an increase in the wet weights during the first days.In the chronic trial the wet weights stayed behind those of healthy control animals.

In the lungs we observed on the first days an albuminoid fluid within the perivascular and parabronchial spaces.During the following days this fluid escaped into the neighbouring alveolar spaces where it is resorbed by pneumocytes which thereby change into foamy cells.The lung vessels exhibit an extreme vacuolization of the smooth muscle cells thereby rupturing sourrounding elastic fibers.By measuring the perivascular and parabronchial spaces we found a regression line which follows y = 0,62 - 0,01x.

+ Granted by Deutsche Forschungsgemeinschaft.

PRIVACY ASPECTS OF DATA-BANKS IN PATHOLOGY

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Analysing the privacy aspects connected with the composition, the use and the fate of the medical records in databankprocedures, apparently the dual privacy of patient and the physician are involved.

The validity of some postulations will be reviewed e.g.:

Databank content regarding a patient can be divided in categories or degrees of hardness, with a corresponding degree of accessibility.

Acceptibility for the participating pathologists and for the patient has to be ascertained through the offered safeguards for their privacy, including various rights of appeal regarding the correctness, mode of distribution and utilisation. The procured information should not be linked to other in an attempt to construct conclusions which will be held against anyone of them.

The choice for the hardware-arrangement has three possibilities. Privacy matters are at risk with each form but in a different way and depending on the possibilities of non-corrosive guarantees.

CHANCES AND PROBLEMS OF COMPUTERISATION IN EPIDEMIOLOGICAL PATHOLOGIE

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The epidemiological pathology is based on the following premises:

1. Autopsy diagnosis, 2. Formalized record, 3. Pathoanatomical thesaurus, 4. Pathoanatomical comparison of the findings, 5. Multivariate methods of pathoanatomical statistics.
Aided by qualified record-linkage-systems the following additional data are seizable:

1. Clinical findings, 2. Psycho-social inquests, 3. Socio-ecological data, 4. Biographical data (individual, social and ecological anamnesis).

Some examples show to what extent the statistical analysis of heterogene data collectives do allow or do not allow a binding statement within the range of epidemiological pathology. There are a lot of organizational, instrumental, scientific-theoretical and branch specifical criteria, which are to be fullfilled.

IMAGE PROCESSING IN PATHOLOGY

Kunze,K.D., Arnold,F., Herrmann,W.R., Kemmer,C., Meyer,W., Recknagel,R., Wagner,H., Voss,K. and Simon,H.
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The paper deals with our attempts at image processing in cytology and histology. This attempts includes the automatic analysis of cervical smears for cancer detection and morphometric investigations of light and electron microscopic pictures of liver tissue sections. With the aid of a flying-spot scanner the pictures are represented as two dimensional arrays of gray values. The digitized images are processed by computer programs. Special programs are developed for eliminating artefacts, inflammatory cells and debris in images of cervical smears. In other programs a number of parameters is derived from features that are normally recognized by human observer, such as size, shape and chromatin distribution pattern of liver and squamous epithel cell nuclei. This features are capable of classifying the objects. Results of classification are the basis for diagnostic evaluation of cervical smears and for an exact morphometric description of classified objects in liver tissue sections. From our investigations it can be concluded that there is a lot of applications of image processing in pathology, which can reduce the tedium of repetitive operations or improve their accuracy.

HISTOLOGICAL,MORPHOMETRICAL and STATISTICAL INVESTIGATIONS IN HEARTS and KIDNEYS OF RATS AFTER THERMOCOAGULATION OF THE THORACIC DUCT BEFORE THE LEFT ANGLE OF JUNCTION.

N.Müller,H.Cremer+,J.Tantow and R.Nienhaus
Institute of Pathology and Dept. of med. Dokumentation,Statistik and Datenverarbeitung der Medizinischen Fakultät,University of Bonn,GFR.

In the heart an albuminoid fluid fills the perivascular spaces and the spaces in the connective tissue.After the 2nd day disseminated myocardial necroses occur in the outer two third of the myocard By measuring the perivascular spaces we found a dilatation during the 1st-3rd day (regression line - y=0,63-0,015x).The dilatation vanishes until the 23rd day.The statistical studies of the wet weights of the hearts show an initial increase of the heart weights which are followed by a decrease as compared to the wet weights of the hearts of the healthy control animals.

In the kidneys we observed a dilatation of the perivascular spaces together with a vacuolization of the cytoplasm of the tubules that neighbour the dilated perivascular spaces.Simultaneously protein casts appear in urine.There are no lymphatic capillaries in the medulla or the renal capsule.By measuring the perivascular spaces we found a marked dilatation during the 1st-3rd day which is followed by a moderate collapse until to the 23rd day.The statistical studies of the renal wet weights show an initial increase of the weights as a result of fluid storage.In the chronic trial the renal wet weights stay behind those of the healthy control animals. +Granted by Deutsche Forschungsgemeinschaft

STRUCTURE AND DEVELOPMENT OF A THESAURUS FOR ACCOMODATION OF AUTOPSY AND BIOPSY RECORDS TO AUTOMATIC FREE TEXT EVALUATION.

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Institutes of Pathology, Neuropathology resp. Frankfurt, Hannover, Berlin, GFR,Bern,Switzerland, Vienna, Austria and Department of Medical Informatics, Medical Academy Hannover, GFR

This thesaurus is the second stage of a system developed in Frankfurt and Darmstadt. It is basing on special retrieval experiences with the former system and on the cooperation of several European institutes with different nomenclature and with different primary data processing. The system is dealing with the single elements (words) of diagnostic sentences defining in medical records different morphological findings as well as different physiological and chemical disorders or alterations. During automatic classification at first the words pass a kind of filter eliminating variants due to different spelling (mixed language!) und then reach the "entry" of the thesaurus. Here 25 000 formally different words are reduced to 8 500 substantially different terms, classified according to their substance as " findings ", " anatomic site " and "modifiers ". In a correlative system superordinate terms and enclosed basic terms are added to come to a complete automatic retrieval without narrow terminologic contr.

HISTOPATHOLOGICAL DEFINITION AND CLASSIFICATION OF TUMOURS.

Sobin,L.H., Path.Inst.d.Univ. Geneve-Switzerland.

VARIATIONS IN THE STRUCTURE OF INDIVIDUAL TESTICULAR TUMOURS

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The variations in histological structure of individual germinal testicular tumours have been studied in a series of 24 tumours obtained entire by application of the step-section method. The number of blocks ranged from 3 to 60 depending upon the size of the tumour. One section from each block was classified according to the "American" system, introduced by Friedman and Moore. Eleven tumours were classified as pure seminomas. Seminomatous areas were also observed in two of the five embryonal carcinomas: the numbers of such sections were 18/53 and 2/60. Teratocarcinoma was diagnosed in eight cases. In three instances, sections containing embryonal carcinoma only were noted: the numbers of such sections were 4/17, 6/31 and 15/57. Seminomatous tissue was found in three teratocarcinomas. In the classification used, seminomatous areas do not alter the diagnosis of embryonal carcinoma or teratocarcinoma. A comparison was made between the reclassification diagnoses made in respect of the original biopsy specimens, and the final diagnoses made on investigation of the whole tumours. The two diagnoses corresponded in all 24 cases.
It may be concluded that the Friedman-Moore classification of testicular tumours is well suited for clinico-pathological studies, even if no more than one or a few tissue specimens are available.

APPROPRIATE ACQUISITION AND RECORDING OF PATHOLOGY DATA AS A PREREQUISITE TO USEFUL INFORMATION RETRIEVAL

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Data processing in autopsy or surgical pathology does not require for storage and retrieval an equipment different from the one used in other disciplines. Therefore the paper refers predominantly to acquisition and primary recording, because within this phase the peculiarities of the matter can be demonstrated best, based on examples from the literature and own experience. Special regard deserve the facts that the data come from different sources and that they are mainly the result of observation or inquiry, less of measurement. The statements imply changing quality and quantity of data and a great number of non-numerical characters per case. Kind and sequence of data, possible selection or reduction must be considered in detail before appropriate forms for entry of free text and/or coded data can be designed. If the first step of data processing is not planned and realized carefully, the retrieved information will not hit the needs of the user, not even with the aid of a large-sized computer.

SNOMed-THE COMPUTER LANGUAGE OF MEDICINE.

Arthur H.Wells - National Institute of Health Research, London - England.

SNOMed will be constructed by committees of various medical specialties and medical record administrators based on the structural basis of SNOP /1965/. SNOMed will have seven fields of coded terms representing the seven parts of medical speech normally used in describing a patient. These will be composed of those terms used in the various specialties of medical practice arranged in a hierarchical taxonomic structure, using units of information, stressing preferred terms over synonyms yet providing for "intended synonyms." Field trials will be conducted of both SNOMed and the several compendia providing for rapid posting.

By utilization of the encoding expertise of computational linguists automatic computer storage of natural language with its instantaneous retrieval of described bits of information from remote medical departments on a given petient in the process of medical examination is available at terminals scattered through the institution.The final reward is the availability of cross retrieval of any combination of stored medical information needed for clinical research and for compliance with a recently established federal law /PSRO/.

THE USE OF HIGHER STATISTICAL METHODS FOR THE EVALUATION OF THE ORGAN-WEIGHTS FOR AUTOPSY-DIAGNOSIS

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Determination and notation of organ-weights is necessary as there can be drawn from them conclusions on the autopsy-diagnosis. To demonstrate that organ-weights do not depend on age and body-weight only and to have the possibility to correlate six variables or more multiple regression equations were used. For their putting-up higher statistical methods and computer-usage is necessary. The subjects of our study are:
1. The organ-weights of brain, heart, liver, spleen, both kidneys and their relation to age, body-weight, body-height and four groups of causes of death.
2. The weight of the isolated muscle of the left heart ventricle and its relation to age, body-weight, body-height and some constitutional measurements.
3. The organ-weights of the right and left lung, liver, spleen, right and left kidney and their relation to age, body-weight, body-height and some constitutional measurements.
All investigations were made for men and women seperately. Equations are demonstrated.

PHARMACOPATHOLOGY, APPLICATION OF METHODOLOGY OF EXPERIMENTAL PATHOLOGY IN PHARMACEUTICAL RESEARCH

Organized by

BOLLA K.

Invited lecturers

BOLLA, K.
DAVID, H.
FÖLDES, I., FEHÉR, I., NAMÉNYI, J.
GIESEKING, R.
KONYÁR, É., JELLINEK, H.
MAGYAR, K.
SZENDE, B., SZEPESHÁZY, K.

THE SIGNIFICANCE OF PHARMACOPATHOLOGICAL VIEW IN PHARMACEUTICAL RESEARCH

Bolla, Kálmán

Medical Dept., EGYT Pharmacochemical Works, Budapest, Hungary.

Some decades ago the application of morhological methods in the field of the pharmaceutical research, it was practically equivalent witht the specific part of the chronic toxicological investigations, respectively the research of cancer chemotherapy.

Author emphasizes, that the invasion of the modern morphological methods into the experimental pathology provided the opportunity of the developing of the pharmacopathological view. This way became possible to apply the morphological methods both in the pharmaceutical screenings and in the investigation of action of drugs, as well as in the field of pharmacokinetics too. The author give a survey abaut the possibility of the above mentioned screenings. In connection of the pharmaceutical research he deals with the application of the methods, spreeded in the investigation of cellular secretion. He stresses the significance of the pharmacopathological approach in the elaboration of drugs, acting of the respiratoric diseases and other chronic ones. Finally, through the pharmacopathological analyses of the action of mannitol, he demonstrates the use of this view in the investigation of action of different drugs.

DRUGS AND THE ULTRASTRUCTURE OF CELLS

Heinz DAVID, Dept. of EM, Institute of Pathology, Humboldt-University, Berlin-GDR

The examination of the ultrastructure of cells under the effect of drugs is important in two ways:

1. Administering varying doses of drugs in an experiment reveals the potential effect and damage caused by these substances if used as drugs in humans. Alterations in the nucleus or in the organelles are indicative of the metabolic range and/or damaged area in the cell. Qualitative and quantitative changes occurring in certain processes, e.g. in secretion, show the mode of action of the drugs tested. Changes in mitotic activity are evidence of an intervention into differentiation processes. The rate and type of the cells destroyed suggest the toxicity of substances.
2. The use of drugs with a well-defined biochemical behaviour as model substances for investigation into metabolic processes in the cell and its relations with the ultrastructure of cellular components provides an insight into basic processes taking place in the cell. Characteristic changes in the ultrastructure make it also possible to quickly examine the point of attack of a substance whose mode of action is not yet known. Examples for a different mode of action of drugs include cytostatics and antibiotics such as Actinomycin, or Phenobarbital.

AN EXPERIMENTAL SILICOSIS STUDY WITH RADIOACTIVE TRACER TECHNIQUE.

Földes, I., Fehér, I. and Naményi, J.
Microbiological Research Group of the Hungarian Academy of Sciences and Central Research Institute of Physics, Budapest, Hungary

Chronic elimination of quarz particles was investigated using SiO_2 labeled with Na^{22} and given intratracheally to rats. The clearance of quarz from the lungs could be expressed by three exponential components and it was observed that the biological half life of the alveolar elimination proved to be more than thousand days and independent of the quarz dose administered. The relationship between the quarz-load and pathological changes was determined by histological methods and the in vivo observation of the clearance of radiolabeled polystyrene-latex from the lungs. As good correlations were found, the experimental model is thought to be useful for studying the pathogenesis of silicosis.

EFFECTS OF SECRETPRODUCING AND SECRETOLYTIC SUBSTANCES ON BRONCHIAL MUCOSA.

Gieseking, Rotraud
Pathologisches Institut der Universität Münster, BRD

Pilocarpine induces increased mucous formation in the bronchial mucosa of rabbits, so that details of the secretion cycle could be more precisely analyzed. These studies gave no evidence for a transformation of ciliated cells into goblet cells. Goblet cells derive from activated basal cells. This event is associated with a striking stimulation of cell organelles. Early precursors of mucous substances appear in the immediate surroundings of the hyperplastic endoplasmatic reticulum and Golgi-field. During the maturation processes the mucous drops show a progressive swelling and dissolution. These observations gave also detailed informations about the mechanisms of secret-elimination. Examination of human bronchial mucosa from patients treated with Bisolvon showed an increased activity of the submucosal glands. Serous glandular epithelial cells produce lysosomelike granules rich in hydrolytic enzymes. Mucous substances which come in contact with these granules discharged into the glandular lumen show signs of advanced desintegration. These findings suggest that the mucolytic effect of Bisolvon is mainly due to enzymatic processes induced by lysosomelike granules which are in considerably raised quantities supplied under the influence of this remedy.

EVALUATION OF THE EFFECTIVENESS OF HYPOTENSIVE PREPARATIONS IN EXPERIMENTAL HYPERTENSION IN RATS.

Éva Konyár and H.Jellinek, 2nd Dept.of Pathology, Semmelweis Medical University, Budapest.

The effectiveness of hypotensive preparations manufactured in Hungary was examined in rats with perinephritic hypertension produced by the Lőrincz-Gorácz method. The renal hypertension of rats was reduced by Senegyt, Sanotensin, Vincamin or BTF. The same preparations retarded considerably or inhibited the development of fibrinoid necrosis and the development of periarteritis nodosa-like lesions. In the treated group we observed as a result of the hypotensive effect an exaltation of proliferative and reparative processes. It is concluded, that this model is useful in testing the effectiveness of hypertensive drugs and the principles of evaluation of results are outlined.

THE ROLE OF WHOLE BODY AUTORADIOGRAPHY TECHNIQUE IN THE STUDY OF DRUG DISTRIBUTION

Magyar Kálmán

Department of Pharmacology, Semmelweis Univ. of Medicine, Budapest, Hungary.

The method of whole body autoradiography introduced by Ullberg /Acta Radiol. Stockholm, Suppl. 118, 1954/ renders possible a detailed analysis of drug distribution. Its advantage is that by its application the animal tissues are not brought into contact with solvents. Thus dislocation of substances in the sections can be avoided. Generally the technique is used for;

1/ the study of special localization of drugs in the organs
2/ permeability studies of drugs through blood-brain and placenta barrier
3/ following the routes of drug elimination.

When ^{14}C-labelled drugs and 20 μ sections are used two-three weeks are needed for exposure. In spite of several efforts this technique yields but qualitative results. We use the method as a routine procedure in the initial stage of distribution studies of many amphetamine derivatives and analgetics. To investigate organs important in respect of distribution in autoradiographic experiments, worth also applying liquid scintillation technique, in order to obtain quantitative results.

PHARMACOLOGICAL INVESTIGATIONS ON THE PHARMACOLOGY AND METHODOLOGY OF ISCHAEMIC AND HYPOVOLAEMIC CONDITION IN THE CAT BRAIN

W.Meier-Ruge, H.Emmenegger, P.Gygax, O.Hunziker and A.Cerletti

Dept. of Basic Medical Research, SANDOZ Laboratories, Basle, Switzerland

The isolated perfused cat head and the hypovolaemic shock are interesting models to test therapeutic effects on brain insufficiency With these models it can be demonstrated that a wide tolerance of blood flow exists in the brain cortex. The high insensitivity of neuronal cells to a decrease in the blood flow is reflected in morphometric data of the capillaries in the brain cortex. The normothermic isolated perfusion of the head induces a progressive decrease of EEG-activity which correlates well with morphological damages of astrocytes and neurones. Much more distinct effects on structure and function of the brain can be observed by an ischaemic injury on the isolated perfused cat head. An inhibition of these damages can be induced by DH-ergot alkaloids (DH-ergonine, Hydergine etc.). In the models described pharmacological effects of drugs on brain insufficiency can be examined.

MORPHOLOGICAL ANALYSIS OF THE GRANULAR PNEUMOCYTES AND LIPOID MEMBRANE-STRUCTURES IN THE LUNG BY TOPO-OPTICAL AND FLUORESCENT STAINING METHODS

Németh,Árpád

Inst.of Path.Anat.Univ.Pécs,Hungary

So far no microscopic method has been available to demonstrate the pulmonary alveolar surfactant lipoid membranes or the alveolar granular pneumocytes involved in the secretion of alveolar surfactant lipids. These components were recognized and demonstrated by physicochemical and electron microscopic method.

In the present investigations an attempt was made to use polarisation optical and fluorescence methods for demonstrating the pulmonary lipid structures. In the polarisation microscope the granular pneumocytes show a strong birefringence due to their granular lipid content. The alveolar lipid membrane structures can be vizualized by oriented dye binding reaction with toluidine blue which induces strong birefringence of the membranes.

Coffeine-benzpyrene fluorochrom lipid staining was used for fluorescence microscopy. The alveolar granular pneumocytes were found to show a strong fluorescence effect. Both polarization and fluorescence microscopy are valuable means in demonstrating the pulmonary lipoid structures and provide a new possibility for their study in histophysiology and pathology.

CHANGES OF THE GRANULES OF THE TYPE 2 PNEUMOCYTES ON INFLUENCE OF DIFFERENT CONCENTRATIONS OF OXYGEN.

Réffy, A. Józsa, L. Székely, O.

National Institute of Traumatology, Budapest, Hungary

The alveolar surface membran is produced by the granular pneumocytes of the lung. The surface active material is included by the lamellar bodies of these cells. The granules of type 2 pneumocytes and surfactant was examined by electron microscopy on influence of different concentration of oxygen. The quantity, size, form and density of granules were determined as well as the changes of the surfactant were examined. The effect produced by the high oxygen concentration caused an increase in the density of granules and the damage of the alveolar surface membran. The surfactant has shown no alterations after hypoxia treatment, but the number and density of the lamellar bodies were decreased. These changes can be connected with the production and excretion of the material from the granules of the cells.

SOME EXPERIMENTAL ASPECTS OF THE ACTION OF LIVER-PROTECTING AGENTS

Szende,B. and Szepesházi, K.

/1st Institute of Pathol.Anat.Semmelweis Medical University, Budapest, Hungary/

Authors produced liver damage by the administration of carbone tetrachloride, ethionine, tannic acid and thioacetamide. By means of these chemicals a series of basic pathological changes were produced such as necrosis, haemorrhages, fatty change, fibrosis and alterations in the structure of the nuclei and nucleoli.

All those models were applicated in the course of the study of some liver-protecting chemical agents, especially that of aicamine.

It has been shown that the repair of the damages caused by carbone tetrachloride and ethionine was more rapid and complete than that in the case of tannic acid and thioacetamide treatment. The alterations of the lipid and carbohydrate metabolism due to carbone tetrachloride are prevented more easily than those of the nucleic acid and protein metabolism in thioacetamide poisoning. The simultaneous administration of the dameging and protecting agents results in the best protecting effect.

EARLY CHANGES IN MOUSE LIVER AFTER D-GALACTOSAMINE TREATMENT

Tompa, Anna, Mészáros, K., Lapis, K., Schaff, Zsuzsa, Antoni, F., Garzó, T., Szikla, K.

I.Inst. of Pathol.Anat. and Inst. of Medical Chemistry, Semmelweis Medical University, Budapest, Hungary

Authors investigated the liver-damaging effect of D-galactosamine using in vivo and in vitro methods. 1 hour after 1 g/kg i.p. treatment of mice the incorporation of ^{14}C-Leucine, ^{3}H-Valine and ^{14}C-Orotate into liver cell protein appeared to be inhibited. At the same time a marked basophile granulation was found in the cytoplasm of the liver cells. The granules contained also some PAS-positive substance, not digestable by amylase. The severe liver damage, such as hydropic and fatty change, liver cell necroses and lymphocytic infiltration appeared 6 hours after the treatment, remained unchanged till the 18-th hour and disappeared gradually within 72 hours.
Some of these lesions could be abolished by the administration of galactose. It is supposed that galactose competes with galactosamine for the galactokinase enzyme thereby preventing the formation of unphysiological UDP-hexosamines.

THE INFLUENCE OF DRUGS ON VASCULAR LESIONS IN EXPERIMENTAL ARTHRITIS

Vértesi, Csaba

CHINOIN PHARMACOLOGICAL RESEARCH LAB. Budapest IV. Tó u. 1-5 HUNGARY

Blood vessel lesions reflecting the inflammatory and autoimmune processes taking place in the organism can be demostrated in adjuvant arthritis, a generalized chronic disease of rats. This and consequenthly the developing vascular changes are inhibited by various antiinflammatory drugs.

Steroids inhibit cellular infiltration, intimal and connective tissue proliferation and, to some extent, fibrinoid necrosis but they have hardly any effect on thrombus formation.

Non-steroidal antiinflammatory drugs are active against cellular infiltration and thrombus formation. They have but a weak effect on fibrinoid necrosis.

Cytostatics inhibit fibrinoid necrosis, intimal and connective tissue proliferation, the formation of thrombi but have hardly any effect on cellular infiltration.

DIE HEPATOPROTEKTIVE WIRKUNG VON BETAIN-ASPARTAT-INJEKTIONEN.

Wimmer,P., TAD Pharmazeutisches Werk GmbH Cuxhaven - GFR.

Zweck der Prüfungen war es, die intravenöse hepatoprotektive Wirkung von Betainaspartat zu untersuchen.
Bei 14tägiger Anwendung an Ratten wurden keine Toxizitätssymptome beobachtet.Die LD_{50} für 24 Stunden und 14 Tage lag höher als 12,5 ml/kg. Die intravenöse Gefässverträglichkeitsprüfung an Hunden zeigte keine histomorphologischen Veränderungen.
Die leberprotektive Wirkung an Ratten wurde bei durch hyperlipide diät erzeugte Lebersteatosis und bei Leberverfettung durch Tetrachlorkohlenstoff geprüft. Die pharmakopathologische Untersuchung der Leber zeigte eindeutig, dass Betainaspartat i.v. und i.p. eine leberprotektive Wirkung am Tier hat.
Inzwischen konnte auch klinisch bestätigt werden, dass die intravenöse Zufuhr von Betainaspartat eine Leberschutzwirkung und einen therapeutischen Effekt bei chronischen Lebererkrankungen zeigt.

VARIA

REFLUX ESOPHAGITIS IN TRANSESOPHAGOSCOPIC BIOPSY SPECIMENS AND HISTOLOGIC APPEARANCES ON OESOPHAGEAL BLOOD VESSELS

Ačko
Institute of Pathomorphology
Ljubljana, Yugoslavia

In a histologic study of transesophagoscopic biopsy specimens taken from 50 patients we observed that the changes in reflux esophagitis vary microscopically with the severity and duration of the desease. A nonspecific ulcerative inflammation affecting the mucosa and submucosa represents the acute, initial stage and is followed by chronic type of cellular infiltration and progressive fibrosis affecting all the layers of the oesophageal wall. Ulcerations in reflux esophagitis resemble ordinary gastric ulcerations, age being an important factor in the liability to haemorrhage. The risk that severe bleeding will occur is greater in elderly people, which suggests that primary vascular lesions as arteriosclerosis, and hypertension are predisposing factors. An analysis of larger biopsy specimens has shown in specific staining methods the importance of intimal hyperplasia and perivascular fibrosis in the base of a peptic lesion, where the blood vessels are very liable to become eroded, holding the blood vessel open and thus excluding the protective effect of local mechanisms. The duration of the desease and the primary vascular lesions are responsible for arterial obliterative changes, the cicatricial avascularity and how fast the protective occlusion has been completed.

AFLATOXIN AS A POSSIBLE FACTOR OF THE LIVER CHANGES IN CHILDREN.

I.Dvorackova, F.Brodsky, J.Cerman

Aflatoxins are a group of closely related metabolic toxins produced by certains of the mold Aspergillus flavus. The contemporary results of the research show that many food stuffs of the animal and vegetable origin are contaminated by these toxins. Their hepatotoxic and cancerogenic effects have been observed in a number of animal species particularly in the young. Unlike in veterinary medicine, very little is known about their effects in the human. The present report is concerned with liver damage in children, where some evidence of the presence of aflatoxin in liver specimens was given.

THE EFFECT OF ARTERIAL HYPOTENSION ON PANCREATIC TISSUE DAMAGE AND MORTALITY IN ACUTE EXPERIMENTAL PANCREATITIS.

Fodor,I.,P.Németh Éva, Folly,G., Papp,M.
Natl.Inst.of Rheumatol.and Physiotherapy, IInd Surg.Clin. of Univ.Med.School, Inst.of Exptl.Med.Hung.Acad.Sci., Budapest-Hungary.

Acute haemorrhagic pancreatitis was induced by 5 or 10 mg trypsin injected in retrograde way into the rat pancreas.The pancreatitis was complicated by a significant fall of the arterial blood pressure.The trypsin induced pancreatic tissue damage progressed in gravity as well as in extent and the mortality increased significantly when the arterial blood pressure of the animals was reduced to a 60 mmHg level by thoracic duct ligation or intraperitoneally injected dextran. The thoracis duct ligation or dextran solely however did not induce either pancreatic tissue damage or appreciable mortality. The authors suggest that release of vasoactive substances in the trypsin treated pancreas results in arterial hypotension which is reduced to a lower level in the dextran treated animals due to disruption of mast cells or in the rats with thoracic duct ligation due to increased pancreatic release of vasoactive substances.The arterial hypotension reduces pancreatic blood flow and the latter makes organ tissue damage progress which in turn elevates release of vasoactive substances in the pancreas and thus a chain reaction starts.

ENDOCRINE REGULATION OF HYPOXIA

Khmel'nitski O.K. and Medvedev U.A.

Postgraduate Medical Institute, Depart. of Pathological Anatomy,Leningrad,USSR

The study of endocrine regulation under different conditions of hypoxia in man is complicated by the lack of a well developed experimental basis. Functions of the endocrine glands under hypoxia were investigated by a histophysiological method in white mice. Morphometry and different stainings were applied in the histophysiological studies of the epiphysis, hypothalamo-hypophysial-neurosecretory system, adenohypophysis, adrenals, pancreas, thyroid, and genitals.

Resistivity to acute and chronic hypoxia was tested by the removal of a certain gland and injection of hormones. Some biochemical and pathological techniques were used.

All the endocrine glands participate in the reaction to hypoxia. Endocrine status is different under acute and chronic hypoxia. The phenomena of progressive transformation prevail under the former,and those of regressive transformation under the latter conditions. Adaptation to a severe hypoxia is not perfect - it is acquired by the loss of the reproductive function and the reduction of vital activity to the level of hypothyroid states. The hypoxia stress is charscterized by an incomplete manifestation of adaptive potencies of the endocrine system responsible for stimulation of hormonopoesis.

TISSUE REACTIONS OF ALBINO RATS TO EXPERIMENTAL ADMINISTRATION OF BULGARIAN ANTHOPHYLLIT-ASBEST.

Kolev,K., Dept.of Hygiene, Center of Hygiene, Sofia-Bulgaria.

Studies were performed on the fibrinogenic and general biologic effect of intratracheally intraperitoneally intrapleurally or intralienally applied Bulgarian anthophyllit-asbest in albino rats. An attempt is made to elucidate the relationship between the direct effects of asbest on the individual tissues and the differences in the histology of local reactions at the different sites of application. In this context is also discussed the possible biological importance of the chemical-mineralogical structure of the Bulgarian anthophyllit which is different from the UICC-standard.

DATA REGARDING THE PATHOLOGY OF THE VENOUS SYSTEM OF PROSTATIC ADENOMA

Kótay, P., Lakatos, O., Pop, A. and Balogh, E.

Medical University, Departments of Anatomy, of Urology and of Pathological Anatomy, Tirgu-Mures, Rumania

In the case of 30 patients operated for prostatic adenoma, the authors studied the clinical picture, respectively the histopathological picture of the adenoma, that of the trigone and that of the wall of the prostatic urethra, attempting to demonstrate the possible correlations existing between the clinical symptoms and the histopathological modifications affecting the wall of the vein. Based on our investigations, it was possible to establish that in most cases the modifications affecting the wall of the vein were those characteristic of old age or were pathological ones, which may substantially contribute to the venous stasis and this may exercise a considerable influence on the development of the clinical picture (retention, haemorrhage, infection).

THYMIDINE AUTORADIOGRAPHY AS THE INDICATION OF OPERATION OF URINARY BLADDER'S TUMORS.

Magasi,Péter and Jrasch, János

Postgraduate Medical School. Dept.of Urology Budapest, Hungary

We have carried out H-3-thymidine autoradiography of bladder tumors in 52 cases. We decided the type of operation by cell activity, histological diagnosis, lymphography and clinical features. Independently from the histological diagnosis at medium index of cell activity /above 10%/ our choice was the radical operative solution, /Op sec. Coffey and cystectomie/. 28 cases the histological diagnosis was carcinoma papillare but the cell activity index varied between 4% and 18%. At 8 cases the cell activity index was above 10%, but by other reasosns we could do only excision: in all cases there was recidive within 3 months. 4o patient are under supervision more than 1 year without tumor. We think the thymidine autoradiography is a useful, exact method for the biological behaviour of bladder's tumor.

THYROID AGENESIS: REPORT OF A CASE

Rossiello R. and Stefani M.

Institute of Morbid Anatomy, University of Naples, Italy

A case of thyroid agenesis in a 17-year-old female (first case in literature), never treated with any kind of drug, is presented. At autopsy the following anatomopathological findings were detected:thyroid agenesis, hydrothorax, hydropericardium, ascites, peritonitis due to torsion of ovary, bronchopneumonia, cystic ovary, elephantiasis of labia mjora, calculosis of gallbladder and, aortic atheromatosis. The study was focused mainly to the hypophysis that was increased in volume, double more than normal, with concomitant enlargement of sella turcica. Histologically three principle types of lesions were detected in the gland: a)adenomatous hyperplasia;b)remarkable presence of gamma cells; c)lack of evidence of beta cells. Adenomatous hyperplasia is related to functional deficit of target glands and, in the present case, is diffuse and characterised by chromophobe cells. Besides, we believe that beta cells have undertaken the characteristics of gamma cells, loosing their qualities for functional breakdown. It is interesting to note the rarity of the morphologic findings and the patient's prolonged survival.

FIRST FINDING OF SOLITARY CAPILLARIA HEPATICA GRANULOMAS IN MAN FROM CZECHOSLOVAKIA

Šlais, Jaroslav

Institute of Parasitology, Histopathological Laboratory, Czechoslovak Academy of Sciences, Prague

This is the first record of the finding of C.hepatica in man from Europe. The worm was identified in 7 out of 9 cases with solitary liver granulomas. These were situated under the liver capsule and were formed by an accumulation of minute, interconnected, necrotic areas encapsulated by hyaline connective tissue, and mostly calcified. The content of these areas consisted of liver tissue, foci of necrotic exudate and remnants of C.hepatica. The penetration of a single worm into the liver was responsible for the origin of the granulomas. Eggs typical of lesions caused by this worm were not present, because it did not complete its development.

SOME DATA TO THE SO-CALLED"GLIOSARCOMAS".

Slowik,Felicia and Zoltán,László

Institute of Neurosurgery,Laboratory for Pathology,Budapest,Hungary

The combination of glioma and sarcoma has been already well known for many years.Recently there was carried out a reexamination of the nature of those intracranial tumours which contain both sarcomatous and gliogenous elements. Stroebe was the first,who used the term "gliosarcoma" for these tumours.

Our ten cases have a combination of glioblastoma multiforme and fibrosarcoma or one of its subtypes.Different morphological examinations were performed in our cases.The primary tumour seemed to be a glioblastoma multiforme in which the sarcomatous neoplastic growth arose from the adventitia of the walls of the blood vessels.Remote extracranial metastasis has been found in one of the cases.The evaluation of the examinations are going to be discussed.

MORPHOLOGICAL CHANGES WITH SUBCUTANEOUS IMMUNIZATION OF THE RABBITS BY EMMONSIA CRESCENS

Jiří Štěrba

Institute of Parasitology, Czechoslovak Academy of Sciences, Prague; Šikl's Department of Pathology, Medical Faculty, UK, Plzeň, Czechoslovakia

Emmonsia crescens is a biphasic fungus causing adiaspiromycosis in small mammals and in man. The extract from mycelium and both inactivated and growing mycelia were use as antigens for the subcutaneous immunization of the rabbits. The antigens were mixed with aluminium hydroxide cream (Al/OH/3) in the ratio 1:1. The changes were being followed for 1-17 weeks. Massive accumulation of inflammatory cells, with granulation tissue at the periphery, appeared around the injected material. Al/OH/3 alone, without antigen, is rapidly resorbed while pseudoxanthom is being formed. Al/OH/3 with the extract causes far more exsudation; inactivated antigen resorbs in a similar way, but more slowly. While active mycelium is being resorbed, adiaspores from the inoculated aleuriae appear and go on growing in the most part of the focus. Histological patterns are in agreement with immunological findings in various stems of Emmonsia crescens used.

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